THE Journal of the Kansas Medical Society

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NOVEMBER
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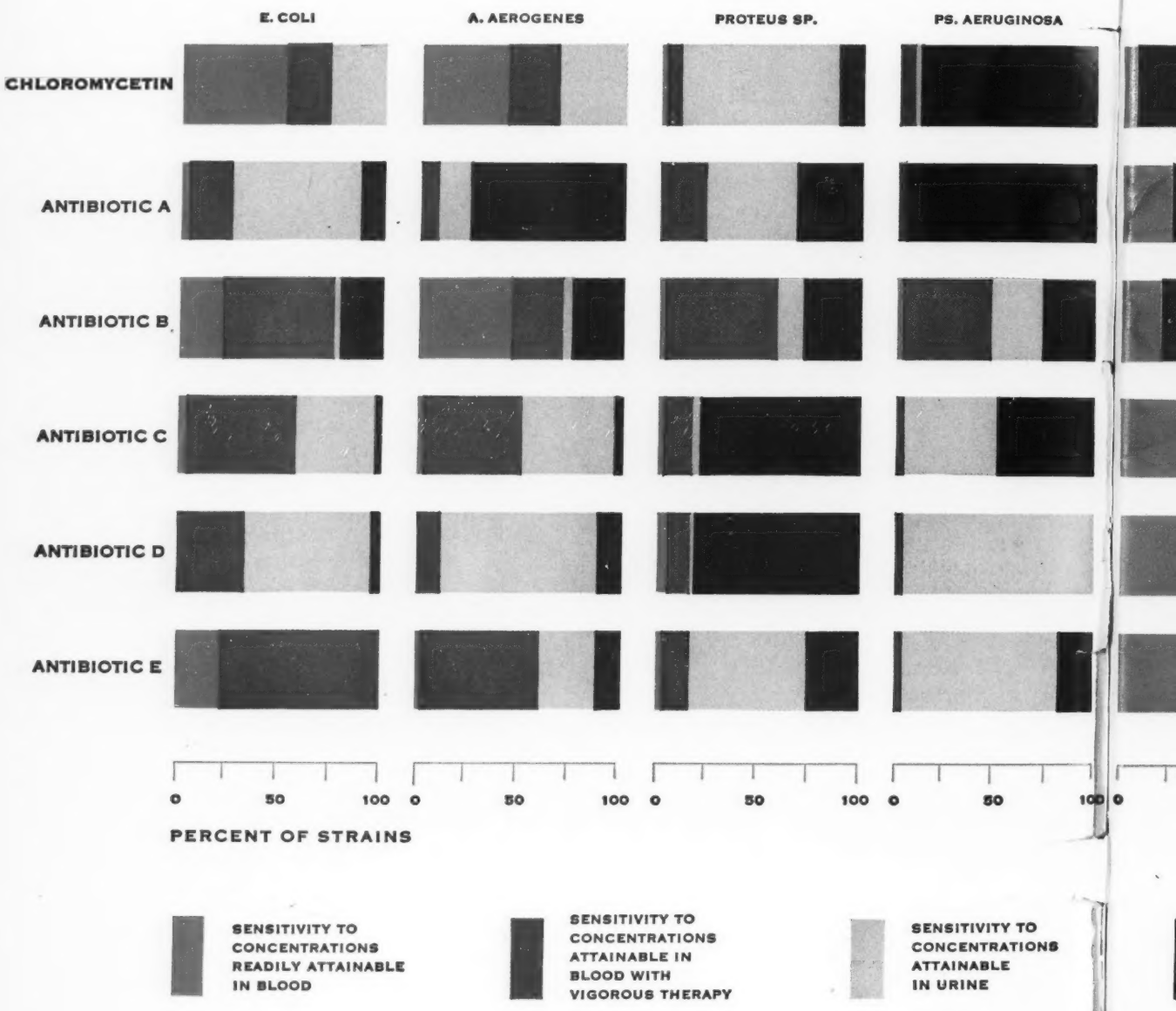
VOLUME 56
NO XI

Resistance of Common Urinary Tract Pathogens to CHLOROMYCETIN and Other Major Antibiotics*



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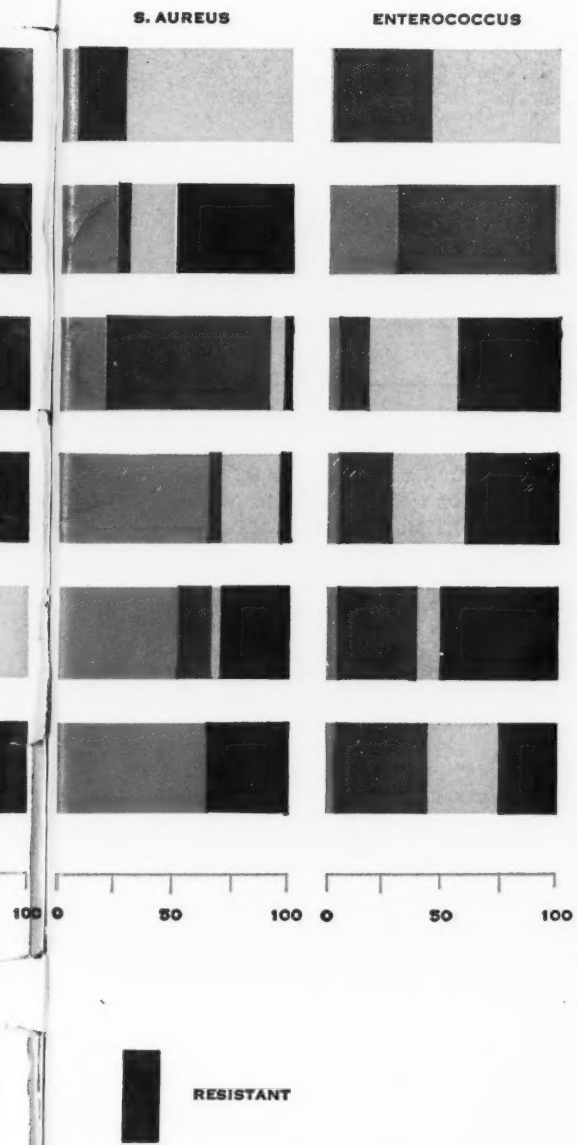

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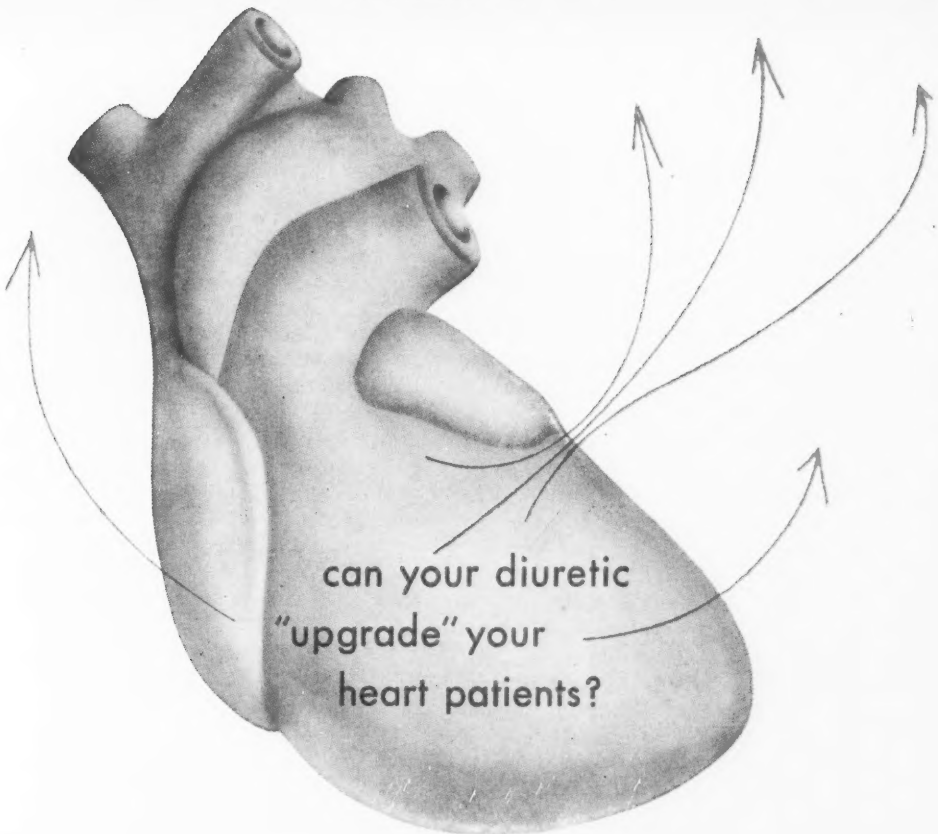

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1. Toverud, K.U.; Stearns, G., and Macy, I.G.: Maternal Nutrition and Child Health, an Interpretative Review, Washington, D.C., National Research Council, Bull. 123, 1950.

2. McLester, J.S., and Darby, W.J.: Nutrition and Diet in Health and Disease, ed. 6, Philadelphia, W.B. Saunders Company, 1952, p. 241.

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6. Bowes, A. deP., and Church, C.F.: Food Values of Portions Commonly Used, ed. 7, Philadelphia, Anna dePlanter Bowes, 1951.

Percentages of Recommended Daily Dietary Allowances* for Pregnant (3rd Trimester) and Lactating Women Provided by 3-Ounce Portions of Cooked Pork Meats and Pork Sausage

	Protein	Iron	Phosphorus	Thiamine	Riboflavin	Niacin	Calories
PREGNANCY (3rd trimester)							
Ham, without bone, 3 oz., cooked[5]	25.0%	17.3%	13.5%	30.0%	10.0%	26.7%	12.5%
Pork Chops, without bone, 3 oz., cooked[5]	25.0%	17.3%	13.3%	47.3%	10.0%	28.7%	10.5%
Pork Sausage, 3 oz., cooked[6]	17.3%	14.0%	9.2%	27.7%	10.1%	18.5%	14.7%
LACTATION							
Ham, without bone, 3 oz., cooked[5]	20.0%	17.3%	10.1%	30.0%	8.0%	26.7%	10.2%
Pork Chops, without bone, 3 oz., cooked[5]	20.0%	17.3%	10.0%	47.3%	8.0%	28.7%	8.6%
Pork Sausage, 3 oz., cooked[6]	13.8%	14.0%	6.9%	27.7%	8.1%	18.5%	12.0%

*Recommended Dietary Allowances, Washington, D. C., National Academy of Sciences—National Research Council, Publication 302, 1953

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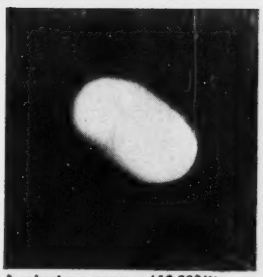

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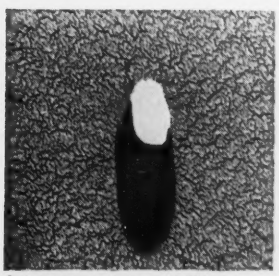

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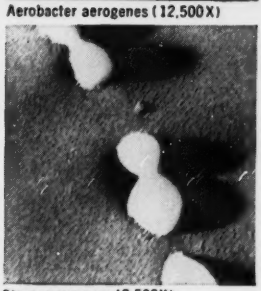

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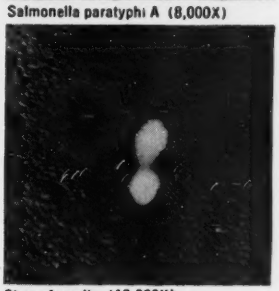

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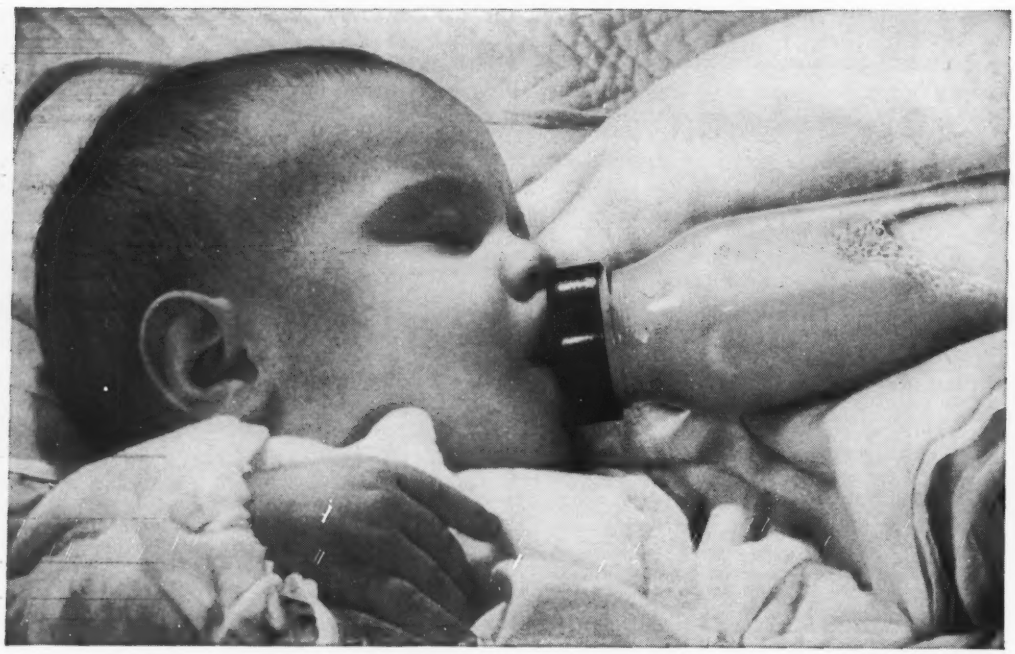

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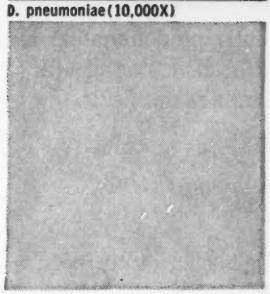

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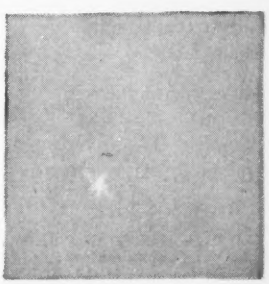

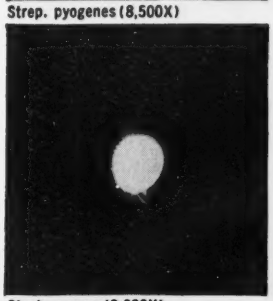

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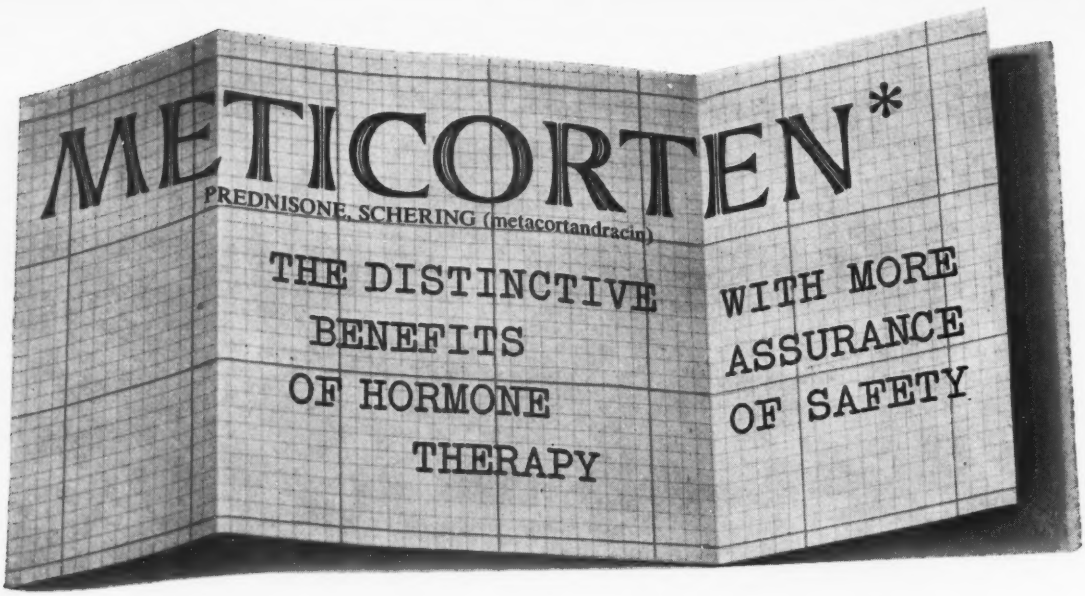

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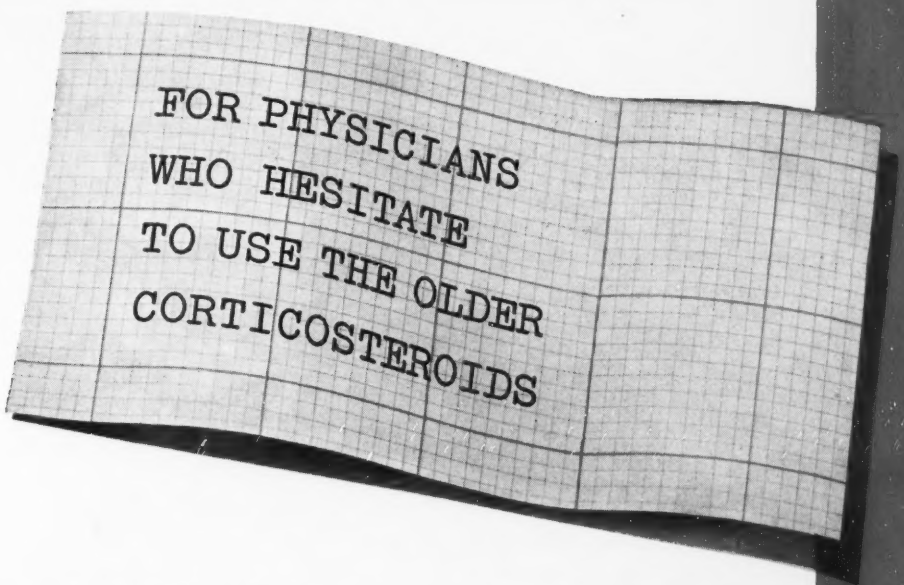

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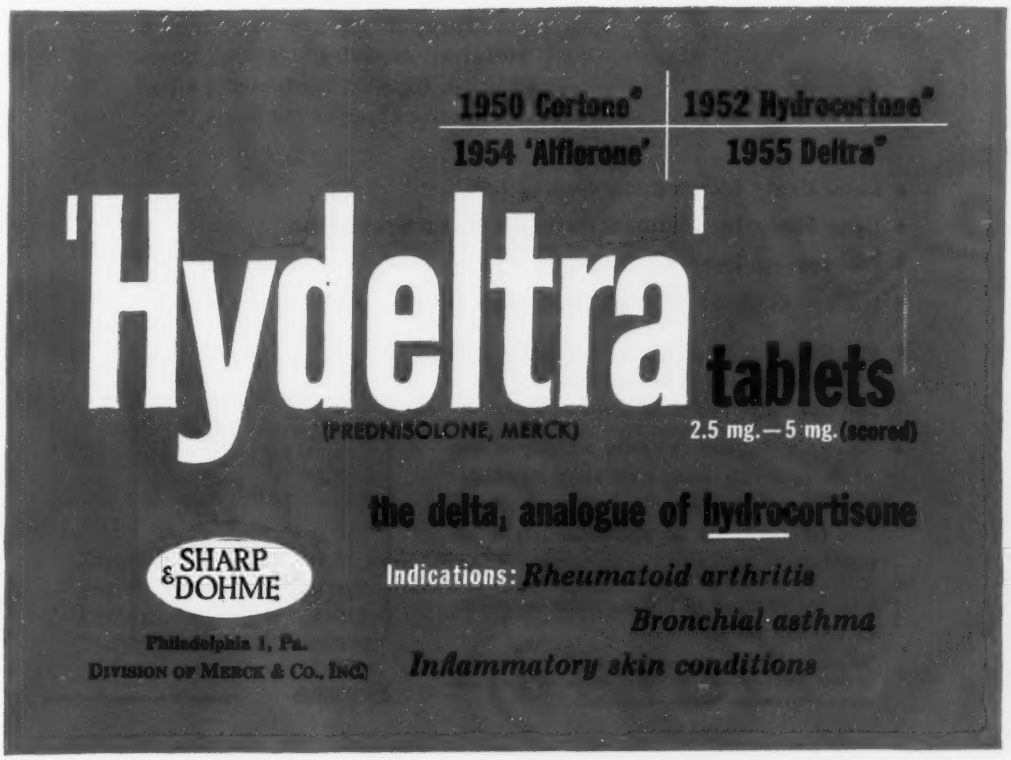

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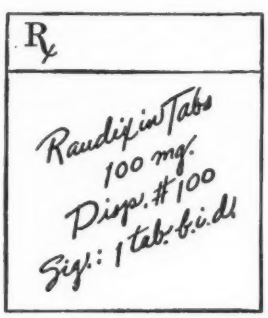

*Ataractic, from ataraxia: calmness untroubled by mental or emotional excitation. (Use of term suggested by Dr. Howard Fabing at a recent meeting of the American Psychiatric Association.)

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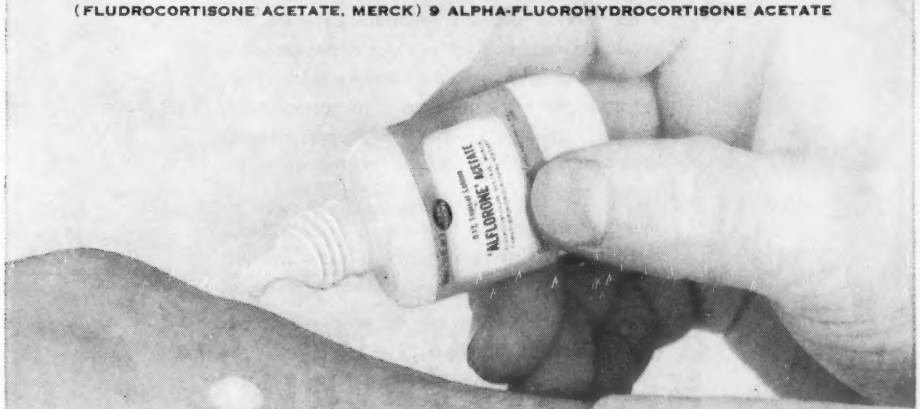

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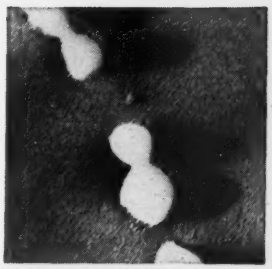
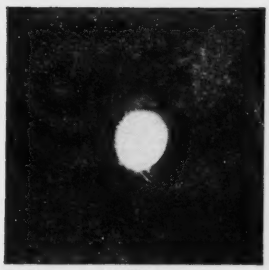
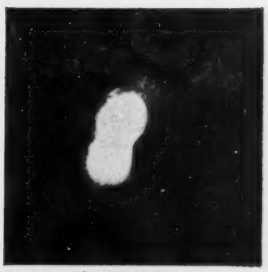


Strep. pyogenes (8,500X)

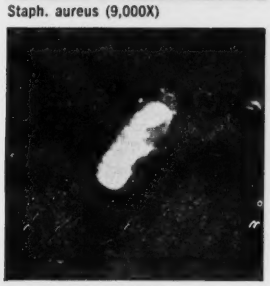


Staph. aureus (9,000X)

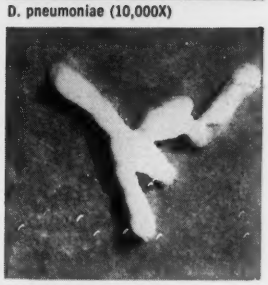


D. pneumoniae (10,000X)

N. intracellularis (5,000X)



H. influenzae (16,000X)



C. diphtheriae (6,000X)

K. pneumoniae (13,000X)

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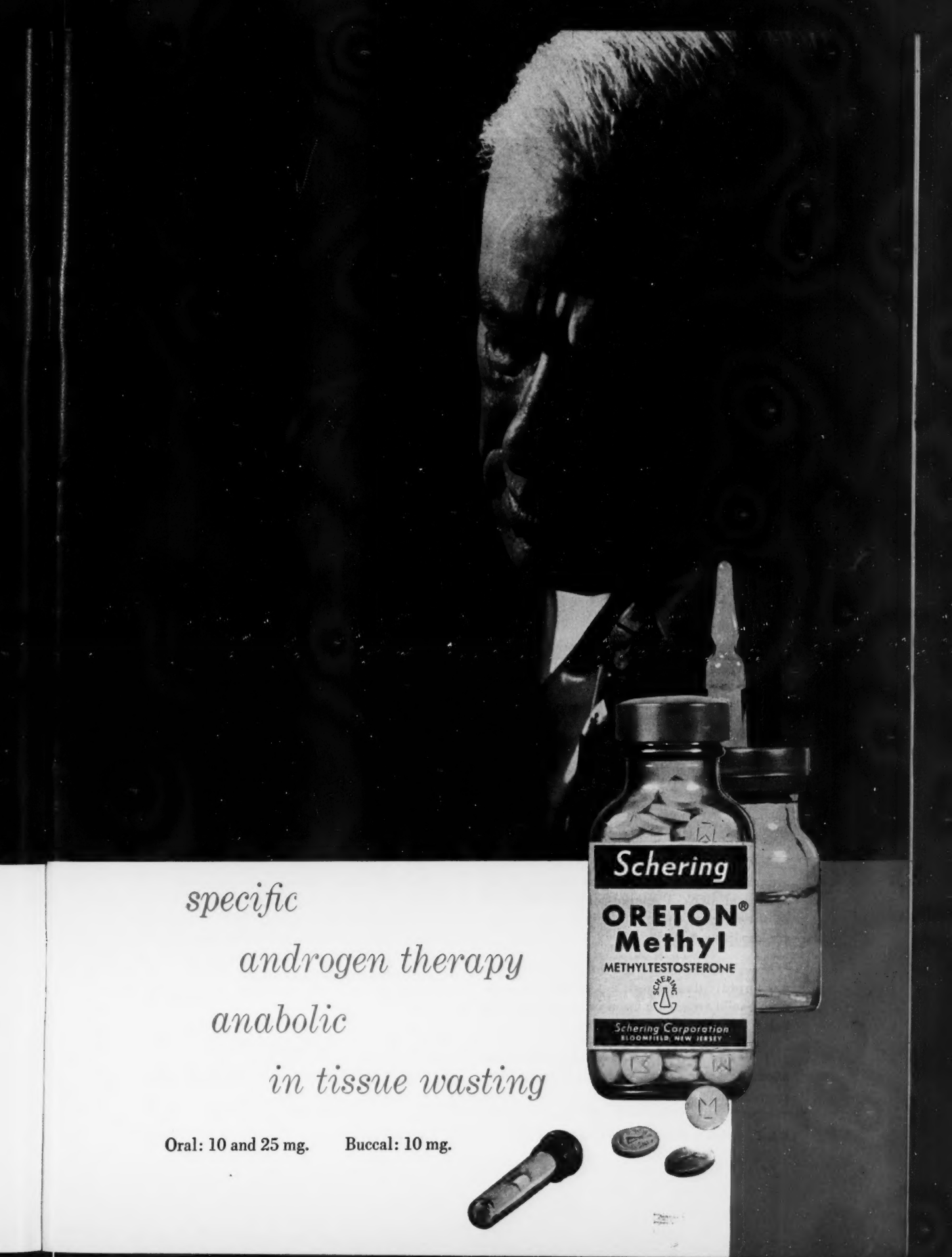

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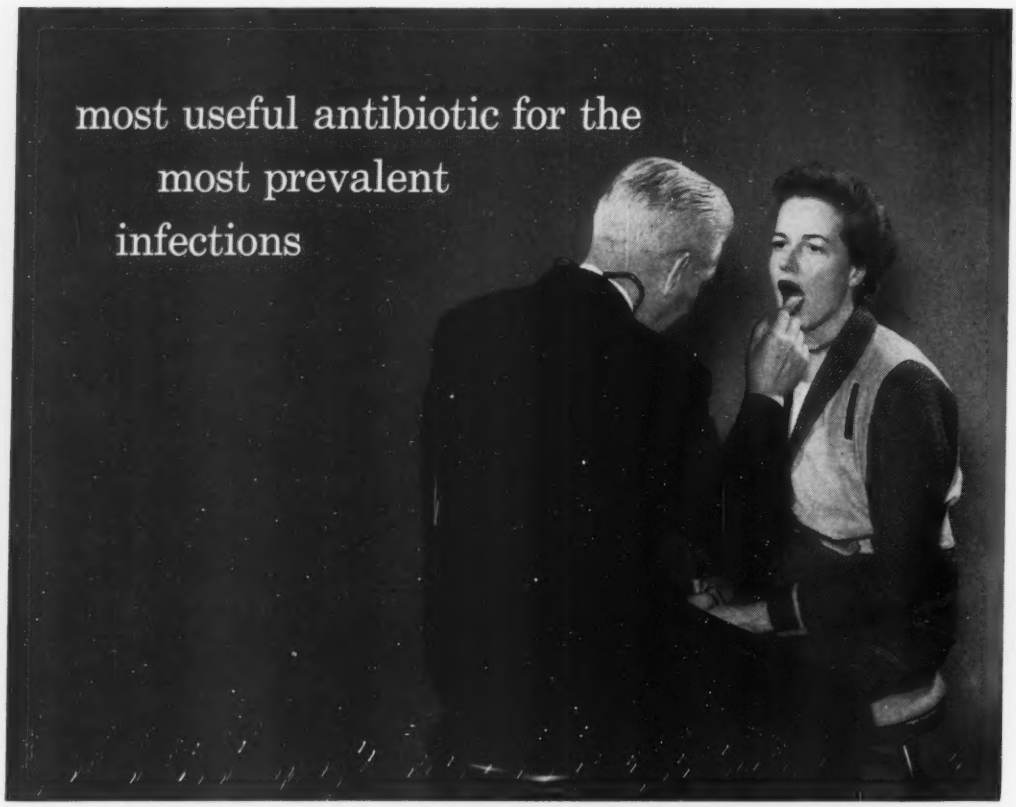

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Volume LVI NOVEMBER, 1955 No. 11

Care of the Terminal Cancer Patient

J. Herbert Nagler, M.D.
Philadelphia, Pennsylvania

The search for a cure for malignancy occupies an important place in the public mind and may be successful in the near future. At a symposium such as this, some day soon, possibly the answer will be announced. Then let us hope such a topic as mine this morning will be unnecessary. Meanwhile, however, patients are suffering with and are dying of malignant disease and require good medical attention now. Basically this is a problem for the general practitioner, because these patients are usually longest under his care.

Last week I saw the latest play by Tennessee Williams, "Cat On a Hot Tin Roof." In it Burl Ives, the noted ballad singer, portrays a wealthy Mississippi planter who has had an abdominal operation at the Ochsner Clinic. It is reported to Ives and his family that the tissue is non-malignant and that his condition is merely a spastic colon. Then the family doctor breaks the news to the household that the tissue is actually cancerous, and at an inoperable stage. It is not important that immediately the family begins to calculate on Ives' death, though this is one of the chief plots of the story. What is significant to us here is that as soon as he finishes the explanation, the family doctor takes out a syringe of morphine to give the patient "because he must be having lots of pain and hiding it."

Ladies and gentlemen, my purpose in coming to you this morning is to plead with you by any words at my disposal not to reach for the narcotic when inoperable cancer is diagnosed.

In this play Burl Ives was his own huge personable self as much after the diagnosis was put into words as he was before. The saying that he had an inoperable cancer did not give him physical pain and did not make him need morphine. He needed medical care, yes, but not dope. No huge sums are required for research in this phase of the cancer problem. You or any other physician can readily apply it.

Patients afflicted with terminal or incurable cancer may be quite active and apparently healthy for months or even years. The diagnosis is not precise, but purely relative, implying only that these individuals have received the maximum benefit of surgery and irradiation, but giving no information on their anticipated years of survival. During the balance of their lives they must be cared for like anyone else, as they may suffer complications of their incurable disease that are not of themselves incurable. These complications may be painful or incapacitating, but they may be quite amenable to routine therapeutic measures.

In recent years a new combination of letters has entered medical terminology. TLC—tender loving care—is recommended for many types of patients. Nowhere in medicine, believe me, can TLC have such fruitful results as in care of terminal cancer victims. Properly applied TLC can inspire a person doomed to an early and painful death to live again, and happily. Many splendid scientific advances can be applied, but the will to apply them, accompanied by TLC, can work miracles. It is amazing that this condition, apparently 100 per cent organic, should have such a large psychic component.

Let me tell you about Norman A. This young man, about 30 years old, was admitted in December of

Presented at the Seventh Annual Mid-West Cancer Conference, Wichita, Kansas, March 25, 1955.

1953 from the Orthopedic Service of one of Philadelphia's fine medical schools. He had been diagnosed as having osteogenic sarcoma of the thigh with multiple metastases to the lungs. He was bedridden, and we were told he had a life expectancy of one or two months. He was receiving 6 to 12 doses of morphine or substitute daily and sedatives in addition. He had a stinking ulcer, about 5 by 10 centimeters, penetrating into the bone marrow, on the anterior surface of the right lower leg, just below the knee. The first slide* shows his chest x-ray on admission, the second his lower leg. On this evidence, plus his clinical record, you can readily accept the hopeless prognosis.

Treatment consisted of gentle irrigation of the cavity daily or every other day, then lining it with crystals of urea. Gradually the cavity filled in, and now, 15 months later, looks like this (third slide). Meantime he was weaned off narcotics rapidly, in about two weeks was out of bed in a chair, in six was standing, and now he looks like this (fourth slide). His chest x-ray looks like this (fifth slide), showing, as you will recall, no significant change. My biggest problem with him right now is that when I want to see him he is often downtown at the movies, and we are beginning to have considerable doubt about the diagnosis.

Care of these patients is probably hampered by the physician's resentment at being unable to effect a complete cure. Here, as almost nowhere else in medical work, the physician must aim for somewhat less than a perfect result and must learn to treat what he can.

Like any other type of medical problem, care of terminal cancer patients divides into diagnosis, treatment, management, and prognosis. None of the principles involved is earth-shaking or new; we must apply to these unhappy individuals rules all of us learned in medical school. But we should apply certain methods that many of us have been inclined to neglect just because of our own sense of futility. The medical literature is scanty, most articles in regular journals having been contributed largely by theologians and social workers, but the small bibliography available is quite satisfying, including a fine article in your state journal by Dr. Ralph Jordan of Holton, Kansas.

As in the handling of any other disease state, the first step is accurate diagnosis. This divides into two parts; confirmation of the diagnosis of malignancy and decision as to whether all other factors are or are not related to the basic disease. The first step should be undertaken by any physician entering the case for the first time, and must include tissue microscopy if at all possible. No other diagnostic method, no matter how obvious or certain, is acceptable, because clinical, surgical, or radiological diagnosis may be incorrect. Particularly today, when so many of the granulomatous lesions are amenable to specific therapy, it is important that a pathologic diagnosis be absolutely insisted upon.

The second phase of diagnosis, as to whether intercurrent disease is related or unrelated to the underlying malignancy, is also fundamental. Frequently treatment by readily available measures may provide rapid and complete relief. Edema, which causes pain and interference with function, may be due to the disease process, but it may also be due to some circulatory pathology; pain may be caused primarily by the neoplasm or may result from secondary infection of the growth, but it may also be stimulated by any other intercurrent condition. When a precise diagnosis can be made, it is often possible to help the patient considerably with regard to many if not all of his complaints.

In general, it may be stated that pain directly due to a malignant process, except a pathological fracture, is of rather gradual onset and is fairly fixed in location. Pain caused by other conditions may be of sudden or gradual onset and may be more transient, depending, of course, on its cause.

Many of the patient's complaints may be due not to the tumor itself but to irritation or secondary infection of the tumor. Particularly in hollow organs, and most particularly in the gastrointestinal tract, the continual passage of contents may cause irritation and secondary infection that makes the tumor noticeably larger. Edema of extremities may mimic metastatic involvement of spinal nerves, fluid in chest or abdomen may act similarly to solid masses in the same areas, etc. These developments should be reevaluated in each patient at rather frequent intervals.

Treatment is probably best begun by an intensive effort to eliminate narcotics if at all possible. This is imperative because in almost every case it will be found that either the physician, the nurse, the responsible family member, or the patient himself has been overdosing with oral or parenteral pain-killers. Narcotic addiction of itself causes anorexia, malaise, weakness, and not infrequently abdominal pain or cramps, and often these are incorrectly attributed to the malignant process. It may not be too apparent that the patient has become an addict, because he may obtain relief from one of several drugs, whereas the true addict usually prefers only one or two. Weaning him away from his addiction may be quite difficult, and again is hampered by the physician's own feeling of futility. "Why," he may ask himself, "deprive the patient this bit of relief?" The answer is that in practically every case the patient will feel better, not worse, after he is free of the narcotic.

The easiest way to reduce narcotic consumption is to give progressively smaller doses, at progressively

* The presentation of this paper included the showing of slides not available for reproduction here.

longer intervals, often by adding atropine, and finally by administering sterile water or an oral placebo. In a matter of only a week or two the patient is ready to be told that he need have no pain-killer—and this frequently gives a tremendous psychological boost.

A particularly pathetic aspect of the terminal cancer problem is the stinking ulcer or superficial lesion, characteristic in appearance and odor, regardless of the underlying pathology. This not only disturbs the patient himself but frequently antagonizes would-be visitors. Treatment begins by cleansing. For some years we have gently cleansed these areas with soap and water, then spread crystals of urea freely over the area. This material may occasionally be irritating to the surrounding skin, which though unbroken is rarely normal, and so vaseline or aluminum paste may be applied around the ulcer. It will be found that urea causes a liquefaction of the ulcer debris, and the loosened debris should be removed by washing with soap or detergent. We have not found any of the newer debris solvents, such as streptokinase and streptodornase, trypsin, etc., any better. After three to four weeks of such treatment the entire area should be painted with 5 to 10 per cent silver nitrate daily for about one week, then the urea crystals should be used again.

Secondary infection should be treated by appropriate antibiotics. Patient application of this method for several months of steady though slow progress may see a huge, indescribably ugly ulcer remarkably improved or healed. If any of the local procedures is too uncomfortable, the area may be first chilled with an ice-bag for 15 or 20 minutes, and occasionally the ice-bag may be reapplied after treatment. Cleansing of the superficial ulcer and elimination of secondary infection on external lesions or those involving hollow organs may cause considerable reduction in tumor size and thereby considerable amelioration of symptoms.

Any odor remaining may still be quite distressing to the patient and those around him. It may frequently be removed almost completely merely by changing dressings frequently in addition to the methods just mentioned. If some odor still remains, it may be adsorbed by animal charcoal prepared in small sachets about 4 inches square and kept close to the odoriferous area for 6 to 12 hours, then allowed to air out for twice as long. About six such sachets, used two at a time, will help a great deal to reduce obnoxious smells.

Very frequently, when the surface debris has been removed, it is desirable to have a re-evaluation by the radiologist and the surgeon. The former may help in further relieving secondary infection, if it is still present. Moreover, when the patient's life has been extended for an unanticipated number of months, it may be that he has lived longer than the originally calculated tissue tolerance and may again be a candidate for irradiation. The surgeon too may reconsider his decision not to operate when he sees a more circumscribed lesion in more healthy surroundings. It must never be forgotten that irradiation and surgery are still the only proved modalities that can actually destroy cancer.

Abnormal collections of fluid, whether interstitial or in normal body cavities, must be removed if at all possible. Many cases respond to oral or parenteral diuretics. Edema of extremities, such as in an arm following radical mastectomy, may be relieved by application of elastic, non-adhesive (Ace) bandage, which should be removed and reapplied whenever it becomes loose, even every four to six hours at first. If swelling involves the individual fingers, one-inch strips of the same bandage may even be applied around each individual finger. The toes need not usually be so individually handled. The edematous part must also be elevated, even if only by two or three inches, as much of the time as possible. It is even justified to have the patient remain in bed for a day or two so that the extremity or extremities involved may be elevated on a pillow or suspended from an overhead sling.

Collections of fluid in pleural and peritoneal cavities should be removed as often as necessary, and occasionally it will be found that deposition of the fluid suddenly slows or stops completely. One patient with lymphosarcoma, who had more than 50 abdominal paracenteses in the next-to-last year of her life, lived a whole year after the last tap was required; and a postoperative mastectomy patient presently under treatment required six thoracic paracenteses from two to six weeks apart, yielding 500 to 2,600 cc. up to eight months ago, but has required none since. Recently she has responded well again to Thiomerin.

More specific therapy is directed against specific neoplasms, and here I have little that is new to contribute except to say that if you are going to use a specific, use adequate doses. Stilbestrol (10 mgm. three times a day) will help about 80 per cent of prostatic cancers; testosterone (50 mgm. every second day) will help most patients with inoperable or metastatic disease originating in breasts, ovaries, or cervix; nitrogen mustard may be of benefit in the lymphomas, I-131 or the thiourea group in thyroid malignancy, etc.

Recently I have used hydrocortisone in doses of 25 mgm. three times daily with great improvement in the patient's subjective state, and such subjective improvement may work a miracle on the objective condition. Other materials have been used, have fallen largely into the discard, but occasionally still may be useful. These include, as typical examples, cobra venom and the pteroyl group, but there are

many others. All I can say is that as of this moment I know of no magic cure, unless again I mention tender loving care.

It must never be contended among physicians that any of these procedures cures cancer, but any of them may do almost as well by making the patient feel better and may readily prolong the patient's useful life. To the patient, however, any purely temporary improvement must be built up as a potential or beginning cure. Moreover, in cases where some specific such as a steroid inhibits the disease for months or years, it may be difficult even for the critical physician not to become too enthusiastic.

Relief of pain need not be accomplished only by narcotics. Local infiltration of tender areas or nerve block may be of great value. By alleviating pain without causing the depressive effect of narcotics, we may give the patient a tremendous and remarkably long-lasting lift. We use 1 per cent Novocain without adrenalin, in amounts up to 20 cc. at a time, depending on the situation.

Pain relief may also frequently be quite feasible by administration of cold. Ice-bags may be applied directly to the painful area and may frequently decrease pain in a matter of minutes. If possible the ice-bag should be kept on the part around the clock. If more intensive cold applications are attempted, it may be necessary to give one mild dose of narcotic or sedative when they are started, as an early phase of the chilling process may be quite uncomfortable. Then the entire body or an involved part may be immersed in crushed ice for varying periods of time, according to the principles originally laid down by Temple Fay of my city.

The most convenient method of applying refrigeration at present is incorporated in the Thermorite machine. With this device, a part or all the body may be reduced in temperature close to a critical level of 72°F. with splendid and remarkably long-range pain relief. Unfortunately, in the almost two decades since this method was devised and although it is in fairly frequent use in surgery, it has not been used adequately for its original purpose, which was relief of pain for terminal cancer patients.

Incontinence should be controlled—of urine by Foley catheter and of feces by administration of paregoric or similar material. Superficial minor sores should not be neglected, as they may lead to major breakdowns, particularly in areas of contact with the bed. Protection may be supplied by "doughnuts" of soft materials. We have found that a mixture of castor and cod liver oils may maintain the skin's integrity for a long time, and such products as Desitin (zinc oxide and cod liver oil ointment) should be used as required. If possible the elbows should be protected by small adhesive bandages before they become irritated.

This case (sixth slide and seventh slide) is a bed sore, the result of an overzealous cordotomy to relieve the pain of a metastatic carcinoma of the cervix. The patient is paralyzed from the waist down and was admitted with the ulcer penetrating to the bony spine. You can see the healing since her admission in August. We followed our routine of urea crystals and regular cleansing of the area, then kept the ulcer protected with dressings well soaked in a mixture of castor and cod liver oils.

The lesser aspects of therapy of this type of problem deal with the psychology of the patient. In general, it is far better to keep the patient at home as long as his presence does not cause a deterioration of the peace of the household, then as soon as the need arises he should if possible be institutionalized at once. He should be kept ambulatory as long as possible, then, even after becoming bedridden, should be encouraged to sit up out of bed most of every day.

Every patient should be encouraged to help himself in every possible way. Food should be natural everyday foods rather than food supplements, no matter how tasty. Ice cream, hamburger, and juices may provide all the food-stuffs necessary for quite a period of time, yet pass with relative ease through an almost completely closed esophagus. Vitamin supplements should be given in liquid or powder form if necessary and feasible.

The management of these patients includes chiefly intelligent nursing. This care may often be provided by a relative, but it may require a professional nurse. In the home, of course, the responsibility for guidance falls largely or entirely on the physician. In nursing homes, moreover, with their frequent turnover of personnel, it may likewise be the physician's responsibility to be sure his orders are carried out. Orders given to the nurse today are of no value if another nurse is on duty tomorrow. And because so many practical nurses are being utilized in nursing homes at present, we should order not "routine colostomy care," for instance, but "aluminum paste around colostomy area every day."

The surroundings of a terminal cancer patient need not be lonely and gloomy. Provision for companionship and pleasant surroundings should be made at home or away; in fact, the possibility of such companionship may be used as a lure to the patient if he rejects the idea of a nursing home. Of course, the patient should be surrounded by optimism, however phony. This applies to all around him, but particularly to the physician. Every untoward event should be belittled or regarded as part of the disease. Every favorable happening, however trivial, should be built up to its maximum.

When the patient disobeys he should not, as in other conditions, be scolded for non-cooperation. Rather he should merely be told, "If things don't go

well, remember how you didn't do as I told you." For things won't go well and you will need every possible excuse to continue treatment with an intelligent, observing patient. Your failure, impossible to avoid, is concealed by the patient's misdeed.

It is a blessing that although these patients profess great unhappiness and wish for death even when they do not know their diagnosis, they are willing to grasp at any straw of hope they actually feel themselves. The physician who first taught me the care of these poor unfortunates, a surgeon with great experience in oncology, himself died of a laryngeal cancer a few years ago. It was amazing to note, as he went downhill, that he ignored all signs of trouble but grasped at and lived on the most evanescent signs of improvement. Here, as in so many other tragic situations, God blesses the victim with forgetfulness.

We never use the word "cancer" before this type of patient, using instead the euphemisms "malignant tumor" or "chronic ulcer." Our psychiatrist colleagues may call us childish in this regard, but we have been able to have all the cooperation we needed without unduly saddening the patient and have seen great depression induced when the patient learned his diagnosis prematurely. Rather, we allow the diagnosis to "seep in," so that when the patient finally realizes his hopeless state he is too tired to care.

Predicting the future of the patient may demand a degree of precision that is impossible with such a complex disease picture. As may be guessed from what was mentioned before, no hint of prognosis need normally be given the patient. We have been able to have wills drawn and other family matters settled by advising action "just in case" something happens. However, if the patient has somehow learned his diagnosis, one day of life may be quite precious. Who is to place a value on a day of some one else's life? If the patient is conscious and not in too much pain, that day may be worth a great deal to him. Hopeless disease? We all are going to die, some sooner, some later. This patient will probably die sooner, but you and I still may precede him.

With regard to the family, however, such a lackadaisical method may be impossible or inadvisable. Members of the family may have to be summoned from great distances. If they are to remain an inordinately long time, this may cause great hardship, even on a non-breadwinner. The relative may reach the point of subconsciously wishing the patient dead and subsequently becoming severely involved emotionally because he is ashamed of his feelings. We usually keep one relative very closely posted, then try to err, if possible, on the side of optimism, so that the family will continue its day to day activity as much as they can.

In closing, I want to stress again the value of tender loving care in the supervision of terminal cancer patients. If you will give them of your best abilities, you may achieve astonishing results. It seems impossible, as I pointed out earlier, that cancer, probably the least psychogenic of all diseases, should be so subject to the emotions, but it is. Treat these patients as though they were your own loved ones, and the results will amaze you. Your function, I believe, is not merely to drag out the last gasp of the doomed patient, but to permit him to enjoy as much of his life as possible. This is the highest aim and duty of the physician.

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History after all is the story of people: a statement that might seem too obvious to be worth making if it were not for the fact that history so often is presented in terms of vast incomprehensible forces moving far under the surface, carrying human beings along, helpless, and making them conform to a pattern whose true shape they never see. The pattern does exist, often enough, and it is important to trace it. Yet it is good to remember that it is the people who make the pattern, not the other way around.

—*Bruce Catton*

Needed: Wider Medical Interest in Motorist Casualties

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The basic responsibility of medicine with regard to motorist injuries, as distinguished from all other injuries (traffic and otherwise), will always be the active and specific treatment of any and all kinds of these lesions. However, modern epidemiological approaches to these grave problems concerning our public health and safety, as exemplified by so-called human-engineering and crash-impact engineering points of view, are demanding wider and more positive medical participation in current programs devoted to safer motoring.

Since the ever increasing tempo and volume of both ground traffic and traffic injuries offer medicine opportunities to meet this challenge, it is my purpose to converge major attention upon three fundamental aspects of the clinical life history of motorists in general: before crashing, during crashing, and after crashing.

Some aspects of motorist safety are straightforward; a little reasoning makes clear their logic and their application. Others leave pitfalls for muddled thinking with consequent confusions and misunderstandings among the various disciplines and proponents involved. Safety during crashing may fall into the latter class during this stage of transition of motorist safety. Confusion will ultimately be eliminated when nomenclature, definitions, and methods of study are better understood.

Unless the atmosphere is cleared, there will continue to be unnecessary delays toward improved automotive safety design (not to be confused with safety engineering or safety performance of present cars). There will also be waste of money and effort and, most important, a let down along these lines by competent authorities currently engaged in basic, developmental, and field studies on safer motoring.

SAFETY OR SURVIVAL BEFORE CRASHING

Your own safety and that of others in your car depends upon three basic requirements: driver proficiency, good ground surfaces, and safe performance of the vehicles involved. The weakest link, it must be admitted, is the human ingredient. Driver proficiency lags as far behind improved road building as roads are lagging behind automotive engineering.

A reconciliation between human and inhuman ingredients is indicated. This is recognized by studies now being made by Ross McFarland of Harvard, who hopes to achieve a better and safer relationship between design and human performance. Prospective drivers, when purchasing a car, should check factors of visibility and ease of handling in the garage, at the curb, when under way, and when parking.

The educational potential along these lines has barely been tapped. Medical groups stand in the vanguard of those who can orient the public to the basic factors regarding accident prevention, as distinguished from injury prevention. If local, state, and national authorities will demand driver screening, medicine's role will be a pre-eminent as well as an exacting one in establishing adequate medical standards of licensure. The importance of this phase is best learned from a study of accessory diagnoses noted by pathologists when doing autopsies on motorist fatalities.

A study of accessory diagnoses in 26 adults* who had had fatal accidents reveals that many conditions were present which might have had some bearing on the accident. Findings included active rheumatic myocarditis, bilateral cataracts, varying degrees of atherosclerosis (peripheral, cardiac, and kidney), degenerative conditions of various organs, and others.

Psychogenic and other physical factors which could increase accident potential should get more careful scrutiny and evaluation by medical as well as other related authorities. This work should also be coordinated with laws, codes, and enforcement. But, the most important single factor in accident prevention is driver proficiency. This is a matter of driver education of both parents and children at the local community level. The need for support of such programs is urgent. All doctors can participate here, and pediatricians especially can urge parents to educate teenagers in good driving practices and habits.

SURVIVAL DURING CRASH OR UPSET

Among the many human and mechanical variables involved under crash conditions, two common denominators emerge: human tolerance to impacts and crash forces. Both of these elements are best understood from a chronological discussion of what happens under decelerative conditions in both internal and external automotive environments.

The external environment has to do with force and structure alone, except when occupants are forci-

Dr. Kulowski is a member of a special committee of the American Medical Association which is making a study of automotive safety design.

* From the files of the University of Kansas Medical Center, Kansas City, and Missouri Methodist and St. Joseph Hospitals, St. Joseph, Missouri.

bly ejected from the car during the external impact and are exposed to double jeopardy. Internal environment involves interactions between occupants and structures of the compartment. Thus, while the latter is a secondary event, it is primary in so far as human injury is concerned. These statements furnish the key to epidemiological methods of study regarding prophylaxis of motorist injuries, interactions among occupants, car, and highway.

The source of impact often determines the magnitude of the forces involved in the production of injury. This is being carefully considered by crash-impact studies from the standpoint of causative relationships and specific bodily reactions to crash forces. Prevention or moderation of injuries hinges upon this concept. Fundamentally, external and internal environmental events represent absorptions of ungoverned dissipations of energy by structure and anatomy respectively.

The manner in which the automotive structure collapses under crash or upset conditions of deceleration is thought to have great influence on the amount and degree of energies which are transmitted to the occupant compartment and to the occupants. Roth formerly was engaged in research along this line, and Mathewson and Severy of the University of California are continuing that study. The automotive industry is now also carrying on research of a similar nature.

Mathewson and Severy are trying to determine how structures collapse to produce injuries to occupants. They have made some significant observations on front end reactions to full scale barrier impacts and upon anthropometric dummies within crash cars. Roth's original observations on head-on collisions were made after study of stunt driver crashes. These investigations have focused attention upon the tremendous forces evoked under crash conditions, both inside and outside the car, and of their brief duration, hundreds of g's on occupants versus milliseconds.

Medical groups should be aware of these basic contributions to motorist safety, offer their opinions and approval, voice their encouragement, and give scientific and financial support. Undoubtedly such effort will solve some of the present lethal conditions of internal automotive environment in accidents.

It has been found that the tolerance of the human body to high decelerative forces depends not only upon the magnitude of the forces acting upon occupants but also on the direction of the forces, their duration and rate of application, and the area of the body over which the forces are distributed, all of which are highly variable under accident conditions! Medical groups are particularly interested in the latter aspect with regard to survivors and fatalities. It seems to be the most tricky and complex of the problems encountered, chiefly because of lack of valid medical data.

Crash forces are impulsive for the most part but may be inertial or crushing in nature. Fundamentally the limits of factors of safety of the human body are large (DuBois). DeHaven's observations on freely falling bodies and Stapp's work with human volunteers under severe linear decelerative conditions (upwards of 50 g's) substantiate that statement. On the other hand, Sergeant Paul's observations emphasize the low survival quotient of occupants in accidents he felt were survivable. This apparent paradox is being resolved by current investigations on medical and engineering facets of the problem, which would indicate that faulty safety design is the chief cause of death in accidents considered to be survivable ones, crashes in which the compartment was not demolished.

Injuries sustained under crash conditions are best considered under four general categories: (1) topical—lacerations, abrasions, and contusions; (2) skeletal—bones and joints; (3) internal—intracranial, intraspinal, above diaphragm, diaphragmatic, and below the diaphragm, and (4) peripheral—vascular and nerve injuries and complications.

Particularly important is clinical alertness to differences between primary injury and secondary complications as well as to morbidity and mortality from the standpoints of prophylaxis, diagnosis, and treatment. Otherwise, muddled medical thinking is inevitable. The following data resulted from my study of the records of 661 survivors admitted to the Missouri Methodist Hospital, St. Joseph, from late in 1949 until the end of 1954, treated by various members of the medical and surgical staffs. The fatalities reported are from records referred to earlier.

Exposure to motorist injury is universal and ever present.

Among survivors, about 80 per cent had two or more injuries. About 65 per cent received skeletal injuries; 55 per cent contusive and abrasive injuries, and 50 per cent lacerative lesions. Topical injuries far outnumbered those to the skeleton, and internal injuries were relatively infrequent.

Topical injuries occurred chiefly on the exposed parts of the body and most often on the face and head. The neck, chest, and trunk were most often injured in those suffering peripheral trauma. The pelvis and abdomen were definitely less vulnerable. The order of incidence of injury to the various bodily areas was as follows: extremity, head, face, chest, trunk, neck, pelvis, and abdomen. For fractures the incidence order was extremity, face, chest, pelvis, trunk, head, and neck. Internal injuries were most frequent in the head (concussion), abdomen, and chest.

The relative benignity of motorist injuries among survivors is dispelled by a study of pathology in fatalities. The outstanding feature was internal injuries, present in degree in every subject in the series.

From the angle of early death, the chest, not the head, receives the fatal injury. Mediastinal injuries were outstanding, noted in approximately 35 per cent and involving the pericardium, heart, and great vessels. The ultimate limit of bodily tolerances to impacts must be somewhere between those forces which produce internal injuries with survival and those forces which produce fatal internal injuries.

At the other extreme is another basic group made up of those who are in automotive crashes and are not injured at all. They demonstrate the fact that injury is not inevitable under crash conditions and that some features of current design are not always lethal.

Attempts to coordinate features of current car design with specific injuries are being made by several groups, among which are White of Motor Vehicle Research, Dye of Cornell Aeronautical Laboratory in Buffalo, Mathewson and Severy of the University of California, Sergeant Paul of the Indiana State Police, and the Cornell Automotive Crash Injury Research Group working under John O. Moore.

The latter group is undertaking the herculean task of correlating basic clinical and field factors through statewide surveys to accumulate valid statistical data. Working independently, Gurdjian, Lissner, et al., have called attention to engineering factors in the production of head injuries, chiefly skull fractures, and femoral fractures. The fact that skull fractures among survivors do not occur as frequently as had been thought does not deter them from their investigations. They are now studying cerebral concussion, the pioneer work on which was done by Denny-Brown.

The original work on mechanical injuries was done some years ago by DeHaven, who started with a study of plane accidents and later turned to the automotive field, continuing in that pursuit until his retirement. A special tribute is due him for creating interest in automotive safety design.

The researchers mentioned above have implicated certain features of modern interior automotive design as responsible for many injuries, naming especially the windshield, the dashboard, and steering controls. They have also criticized some structural elements of the automobile as a whole on matters having to do with over-all strength and ductility under crash collapse conditions. Although these are problems of engineering and design, improvements must rest upon medical data.

Some contributions to the medical side of these problems were made years ago by Straith, Stuck, Woodward, Beck, and others. Straith classified injuries according to occupant seating and its relation to impact and areas of potential injury. He emphasized guest passenger injuries, especially to those occupying the so-called "death seat," but my observations and those of Automotive Crash Injury Research do not bear out his theory. However, his belief that the back seat is the safest has been strengthened by recent studies, and he was the first to suggest padding the dash.

Woodward's sharp criticism of automotive engineering focused attention upon this aspect of prophylaxis against injuries. The clinical patterns he established have been confirmed by the more recent studies of Snyder.

Several accomplishments can be claimed. These include knowledge of bodily tolerance to impacts under predetermined conditions of force transmission, definite data on the importance of a strong occupant compartment, and information on the practicality of some type of safety barrier interposed between occupants and potential injury areas. An efficient barrier would eliminate the urgent necessity for redesign of the cabin interior.

In considering prerequisites for safety under crash conditions, we must always remember that absolute safety under any and all conditions of crash deceleration cannot possibly be attained. Total safety is the ideal, of course, but students of the problem aim their studies at raising the present low survival quotient. These are the so-called survivable accidents, those in which the occupant compartment is not demolished.

Stapp's experimental observations and DeHaven's analysis of survivors of light plane accidents, with and without safety belts, definitely indicate that belts are well tolerated and prevent or moderate tendencies toward internal injuries. The addition of shoulder harness further increases the rider's security.

It seemed at first that the above statements were contradicted by a study of safety belts made by the American Society of Safety Engineers at Ohio State University, whose research was conducted with the kind of belt worn by window washers. They reported heart injuries in their experimental animals. However, the type of experiments performed and the positions of the animals during force loadings through the belts do not simulate the probable condition of human beings with safety gear under crash decelerative conditions. A clinical paper in a British medical journal several years ago was also derogatory to safety belts, but a restudy of the facts by DuBois refuted the British author's contention, as did experimental work by Bierman and Goldman.

Since the safety belt or its counterpart represents the simplest single adjunct now available for motorists, the medical profession should urge its adoption. That would be a start in the right direction, and advice could be modified or changed at a future time.

The efficiency of such safety gear would be best assured if it were applied at the factory. Its use by the motoring public could be influenced by an intensive educational program sparked by both lay and

professional groups. Physicians could cooperate by reporting types of injuries or lack of injuries to persons wearing belts during crashes (Campbell).

It must always be remembered, however, that without the structural integrity of the occupant compartment, no amount of interior revision, safety barriers, of knowledge of bodily tolerances would enhance survival to any appreciable degree.

SURVIVAL AFTER CRASHING

Despite physicians' familiarity with the effects of crashing, consideration of morbidity and mortality differentials calls for revisions in our concepts of diagnosis and treatment. Four groups of persons are concerned: survivors without injury, immediate fatalities, survivors despite injuries, and survivors who subsequently die of their injuries and complications.

The first group is important to safety designers. They must seek their own clues to these amazing escapes from injury and death.

The mortality differentials, on the other hand, implicate both engineers and doctors.

Immediate fatalities, estimated by Moore to be 15 per cent, represent both extreme and pure relationships between bodily tolerances and crash forces. Increasing the survival rate in this group remains a problem for engineers and manufacturers who have medical and engineering data already at hand. Even here, however, physicians have an interest because of physical conditions present among adults which might enhance death from impacts. Contributory factors as well as mechanical forces are operative all along the line. This factor is especially prominent when considered in relation to intermediate deaths, those within 48 hours of the accident, and the delayed mortality after that.

Before considering specific implications of delayed and intermediate deaths, it is well to consider mortality factors in general. In the Missouri Methodist Hospital series studied, the over-all mortality was 3.4 per cent. This is acceptable and even praiseworthy until the mortality is figured from the standpoint of degree of injury received. Forty-five per cent were considered mildly to moderately hurt, another 45 per cent were thought to have moderate to serious injuries, and 10 per cent were classified as dangerously injured. All of the deaths occurred in the latter group, 34 per cent. If we are to lower the mortality at all, it must be accomplished at this level of injury.

In the present series of deaths, 11 per cent were found dead at the scene of accident, 50 per cent died within 48 hours, most within eight hours after admission to the hospital, and 39 per cent died at intervals as late as eight days after admission.

The number of intermediate deaths focuses attention upon first aid and emergency care. The first is practically non-existent, thanks to current complicated methods and the deterring admonition not to move injured persons until a physician arrives on the scene. It is disconcerting that humanitarian first aid is ignored, despite the fact that many accident victims exhibit obvious fractures of the extremities. It is also disconcerting to learn that attention to such injuries is delayed even after patients have been admitted to hospitals, that they have been submitted to transportation without the benefit of simple splinting or traction.

I suggest that methods of first aid be revised in keeping with increasing needs. This is a responsibility of medical groups. Second, this program should be sponsored by Red Cross and Civil Defense groups, partly as a training ground for possible catastrophic events to come. Third, training in first aid should be given truck drivers, bus drivers, and ambulance attendants who can be counted upon to be available in most instances.

Adequate first aid is the first step in a chain of care. If it can be administered by non-professional persons, physicians can concentrate upon life saving measures having to do with shock, almost always due to excessive internal bleeding, pulmonary ventilation, and cardiac arrest. In some cases a tracheotomy can save the life of a victim with inadequate pulmonary ventilation.

The chief causes of death in the intermediate mortality group in the study were cardio-respiratory difficulties and hemorrhage. Three major complications, pneumonia, fat embolism, and lower nephron nephrosis, worked against survival. Among those who died more than 48 hours after injury, chief causes of death were alterations of urinary output, fat embolism, cardio-respiratory troubles, and degenerative and inflammatory conditions. This implicates definitive treatment, not so much in regard to techniques but more as it relates to revision of therapeutic policy and priorities for the dangerously injured. Risks should be accepted in accordance with the exigencies of individual cases.

CONCLUSIONS

Accident prevention is everyone's problem. Nothing can supersede these common sense objectives. However, this is not enough in itself to stem the volume of traffic injuries and deaths, and it becomes necessary to supplement accident prevention and injury prevention or moderation and improved first aid, emergency and definitive treatment. The responsibility here belongs to medicine, engineering, and manufacturing. Since the problem is multi-faceted, its solution will require an integrated and multi-discipline effort.

In addition to showing professional interest, medical groups are asked to

1. Express approval and support of clinical, basic, field, and developmental research.

2. Step up participation along these lines, especially with regard to furnishing valid data on survivors and fatalities.

3. Increase space in medical journals for education and orientation purposes.

4. Educate patients on the desirability of accident and injury prevention.

5. Present data to engineers in order that they may appraise it from the standpoint of automotive safety design and decide on changes that may be indicated.

6. Encourage and cooperate with their own highway patrols.

The problems of motorist injuries are not at all exclusively surgical ones. Increasing pathologic information serves to point out a need for increasing alertness to the more subtle medical diagnostic and therapeutic problems involved. That in turn calls for more consultation and participation by all medical and surgical specialties, particularly the internist who should be made a member of any team administering to the more serious motorist casualties. Future reductions in the present mortality, expected from improved automotive design, will bring even greater challenges to the medical profession. Are we ready for this probability?

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Radioactive Iodine in the Diagnosis and Treatment of Hyperthyroidism

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TERMINOLOGY

Classification of diseases of the thyroid gland has been standardized by the American Association for the Study of Goiter in the following way:

1. Nontoxic goiter
   a. Diffuse (endemic and adolescent)
   b. Nodular (adenomatous or colloid)
2. Toxic goiter
   a. Diffuse (Graves' disease, primary hyperthyroidism)
   b. Nodular (toxic adenoma, secondary hyperthyroidism)
3. Malignant goiter
4. Inflammatory diseases.

Further subdivision of toxic goiters into such classes as (1) diffuse toxic goiter with exophthalmos, (2) diffuse toxic goiter without exophthalmos, (3) nodular toxic goiter and (4) hyperthyroidism without goiter has been suggested.

This system is urged by those who feel that a clear line of distinction should be made between cases in groups 1, 2, and 4, which may represent pituitary disease, and group 3 which seems to represent a purely thyroid abnormality. Such subdivision is certainly necessary when investigation into the pathophysiology of hyperthyroidism is carried out.

However, in this discussion I shall take the liberty of ignoring the anatomical variations in the thyroid gland, except where specifically noted, and simply use the term hyperthyroidism to designate that disease condition which exists when overproduction of thy-

Mr. White is a student at the University of Kansas School of Medicine. This paper was written during his sophomore year at the school.

roid hormone occurs. I feel this is justifiable since, regardless of the actual site of the primary disorder whether pituitary, adrenal, peripheral tissue, or thyroid, practically all diagnostic and therapeutic measures today are directed at the thyroid gland.

NORMAL THYROID PHYSIOLOGY

Thyroid Stimulating Hormone (TSH)

The function of the thyroid gland is controlled by a reciprocal regulatory system between the thyroid and the anterior pituitary in which a balance between the thyroid hormone and thyroid stimulating hormone in body fluids is maintained. Several factors enter into this arrangement, among which are the production and release of the hormones from their respective glands, the utilization and excretion of these substances, direct hormone interaction, and other factors such as the blood iodine level.[1]

The evidence for the existence of TSH is impressive. Hypophysectomy leads to marked thyroid atrophy which can be reversed by either implantation with anterior pituitary gland tissue or injection of an acid extract of anterior pituitary. In the whole animal, injection of TSH causes marked thyroid hyperplasia with decrease in the iodine content of the gland, rise in blood iodine, tachycardia, increased basal metabolism rate, creatinuria, increased calcium, and all other signs of hyperthyroidism. Although several workers have suggested that no specific TSH exists but that thyroid function is regulated via the adrenal gland,[2] no one yet has been able to produce the signs of hyperthyroidism with any known adrenal fraction.

Isolation, identification, and measurement of TSH have been most difficult for, in contradistinction to thyroid hormone, it exists in such minute quantities that the most delicate bio-assay methods are not uniformly successful in finding TSH in the various body fluids. Two new methods recently described[3, 4] may permit determination of such quantities soon. Such information is of vital importance to untangle the problem of Graves' disease.

While we know a balance exists between TSH and thyroid hormone, we are at a loss to explain the exact site and mode of the reaction. Thyroid hormone diminishes the output of TSH, if production of exophthalmos can be used to measure such output, and so does the administration of sufficient iodine. Direct iodinization of the TSH in vivo reduces its thyrotropic potential greatly. Several hypotheses have been suggested to fit all our present knowledge together. One which is understandable, if not absolutely accurate, is shown in Figure 1.

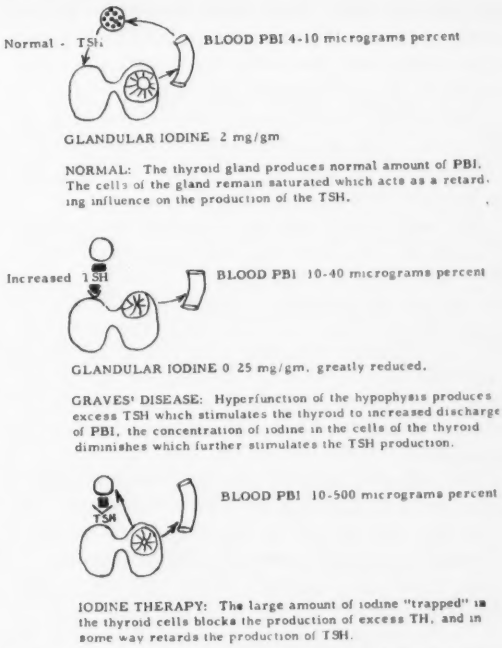
Normal - TSH
BLOOD PBI 4-10 micrograms percent
GLANDULAR IODINE .2 mg/gm
NORMAL: The thyroid gland produces normal amount of PBI. The cells of the gland remain saturated which acts as a retarding influence on the production of the TSH.
Increased TSH
BLOOD PBI 10-40 micrograms percent
GLANDULAR IODINE 0.25 mg/gm. greatly reduced.
GRAVES' DISEASE: Hyperfunction of the hypophysis produces excess TSH which stimulates the thyroid to increased discharge of PBI, the concentration of iodine in the cells of the thyroid diminishes which further stimulates the TSH production.
TSH
BLOOD PBI 10-500 micrograms percent
IODINE THERAPY: The large amount of iodine "trapped" in the thyroid cells blocks the production of excess TH, and in some way retards the production of TSH.

Figure 1. This shows a working hypothesis in which the saturation of the cells of the thyroid, not the PBI or hormone output, is taken as the regulating mechanism of TSH production.

Thyroid Hormone

Thyroid hormone is the only known metabolically active product of the gland, and its production is the only known function of the gland. While there is experimental evidence showing that iodinization of protein can be accomplished in vitro[5] and protein bound iodine (PBI) is found in the blood of completely athyroid animals,[6] suggesting that production of compounds indistinguishable from thyroid hormone may be accomplished in the absence of glandular tissue, certainly the great part of the hormone arises in the gland.

The precise identity of thyroid hormone is subject to great debate. Several workers using fractionation and acetone precipitation studies concluded that thyroglobulin was the active substance.[7] Another group[8] concluded that a thyroglobulin-like substance for which the name thyrenzyme was proposed actually produced metabolic effects in the tissues.

Recent studies concerning the nature of the thyroid hormone in various thyroid states by use of paper chromatography indicate that thyroxine is the final product,[9, 10, 11, 12, 13, 14, 15] and paper electrophoretic studies find thyroxine bound to a plasma globulin component in the circulating plasma.[16]

Thyroxine has also been isolated in the free form in bile and bound as a glucuronide in the gastrointestinal tract by Chaikoff et al.[17] by means of paper chromatography.

An analogue of thyroxine, triiodothyronine, has been recently isolated from human plasma,[18, 19] and

this compound has been found to produce greater calorigenic effects[20] than thyroxine in the treatment of myxedematous persons if it is administered in concentrations below 10 gamma/kg. of body weight.

Our present knowledge of iodine metabolism is best summarized in diagrammatic form showing the various metabolic pathways of iodine. This diagram is illustrated by Thorn et al.[21]

The principal function of thyroid hormone is that of a catalyst acting upon the oxidative processes of the body cells. Tissues from hypothyroid animals have a low oxygen consumption, while those from animals rendered hyperthyroid utilize more oxygen than normal. A secondary function is its reciprocal action upon the anterior pituitary; ablation of the thyroid causes hyperplasia of the pars anterior, degeneration of the basophil cells, and disappearance of the acidophils.

The amount of thyroid hormone produced depends upon the stimulus supplied by the thyrotropic hormone and the amount of iodine available. The rate of production under normal conditions is quite constant; it has been estimated to be 0.35 mg. of thyroxine per day.[22]

Iodine Metabolism, Chemical

The study of thyroid function is almost synonymous with the study of iodine metabolism, for the element is essential to the synthesis of the gland's hormone and has no other apparent function. The minimal daily requirement of iodine in adults is about 25 gamma; however, 100 to 200 gamma is considered more nearly the amount needed to keep an individual adequately supplied, due to variations in absorption. Excretion in the urine of from 20 to 70 gamma a day occurs on such an intake.

The total body iodine is 50 mg., of which 10 to 15 mg. is in the thyroid. Although the amount in the gland is slightly less than one-half the body total, the concentration (2 mg./gm. of dried tissue) is 180 times that found in muscle. As will be mentioned later, this degree of saturation does not exist in hyperthyroidism.

The concentration has been subdivided into inorganic, which is probably dietary in origin, and organic (also called hormonal, protein bound, and precipitable) which represents the circulating hormone.

Although the techniques for determining blood iodine are very complicated,[23, 24, 25] results from competent laboratories show quite consistent values. The most widely used method, that of Chaney,[26] gives a normal range of PBI of 4-8.5, mean, 5.5 micrograms per cent. Values over this are suggestive of hyperthyroidism. This is one of the most specific of laboratory tests, for no other disease causes alterations in blood iodine values.

It should be borne in mind that elevation of blood iodine, both organic and inorganic, will be found following ingestion of iodine in normal people. Average size doses of Lugol's solution disturb the test for two to three weeks. Radiopaque substances are even more confusing, for falsely elevated levels have been found three years after myelography, a year after bronchography, nine months after intravenous pyelography, and three months after cholecystography.[27]

The chemical determinations of iodine substances and iodine concentrations have given considerable information about amounts and types, but with the advent of radioactive iodine a method for the study of movement and function was found.

Iodine Metabolism, Radioactive

As is characteristic of isotopes, carrier-free radioiodine acts chemically and physiologically in the same manner as its natural stable isotope I-127 except for its radiation properties. This has made it possible to measure and observe aspects of iodine metabolism heretofore indiscernible. It should be borne in mind that the mass of carrier-free I-131, 0.00008 gm. per millicurie, is infinitesimal and cannot possibly effect chemical reactions in vivo in the tracer doses used.

Orally ingested radioiodine is rapidly absorbed from the stomach and can be detected in the peripheral circulation within three minutes. Absorption is usually complete within two to three hours, although it may be slightly retarded by the presence of food. Usually not more than 3 per cent and never more than 11 per cent is excreted in the stools. Subsequent to absorption of I-131, the curve of serum concentration shows an initial rapid rise, reaching a peak at about one hour. By this time an exponential fall becomes marked, representing urinary excretion and thyroid accumulation. Finally the serum level approaches a plateau which represents the appearance of protein bound I-131. In case of a continual rise, hyperthyroidism is suggested.

The concentration of radioiodine in tissue other than the thyroid is minimal. No exact figures are available concerning final equilibrium; however, 57 hours after the administration of a large 63 MC dose, the following concentrations were found: muscles 3.3 per cent, liver 3.9 per cent, brain 2 per cent, lungs 0.6 per cent, and kidneys 0.1 per cent.[28]

The isotope is excreted promptly in the urine, over half of it appearing in the urine during the first 48 hours; following this only traces are present.

Practically all the I-131 not disposed of by the kidneys is concentrated in the thyroid.

Metabolism of iodine by the thyroid may be represented as a three-phase process. The initial step or, in other words, the accumulation phase, probably involves only iodide free of protein linkage. The ele-

ment at this stage is merely "trapped" by some mechanism in the form of iodide in the epithelial cells of the follicles and not chemically altered. It appears that this "trapping" mechanism is blocked by KSCN and enhanced by TSH.[29] The ingestion of KSCN will cause rapid discharge of "trapped" iodide in glands treated with these substances but will not influence the amount of protein bound iodine.[30] The next step is the oxidation of iodide to organic iodine by a peroxidase. This oxidation appears to be inhibited by thiourea compounds and sulfonamides.[31]

Simultaneous with the trapping of iodide in the normal gland, peroxidase oxidation of iodide to iodine and conversion to organically bound iodine and accumulation as diiodotyrosine and thyroxine in the colloid occurs. Radioautographs show about 90 per cent of the I-131 in the gland to be in the follicular spaces in the protein bound form 30 minutes after ingestion.[32] No radioiodine was seen in the cells by several workers; however, later workers showed by more rapid extirpation that the iodine passes from the cells into colloid. The exact nature of the hormone in the gland is in doubt, but analysis shows that it is composed of approximately 25 per cent thyroxine and 75 per cent diiodotyrosine.

The third and final stage is secretion. In contradistinction to the trapping and conversion which are quite rapid processes, being completed within two days, the secretion of I-131 in the protein bound form, apparently hormone, is much slower and appears to be under the control of proteolytic enzymes. Very little protein bound radioiodine can be detected in the blood within the first 24 hours, and the level remains quite constant for many days.[15]

ABNORMAL IODINE METABOLISM IN HYPERTHYROIDISM

There seems little doubt that more than one type of hyperthyroidism exists; however, in the light of present knowledge it is safe to say a common denominator exists in all forms, and that is production of thyroid hormone in excess of body needs. Study of the metabolism of iodine in hyperthyroidism with I-131 has shown this to be true.

Absorption of tracer doses from the gastrointestinal tract is not measurably altered by Graves' disease unless severe diarrhea is encountered.[33] The entire course of events subsequent to absorption differs markedly. The hyperfunctioning gland, having a very low iodine concentration, takes up much more of the given dose and at a greater rate than normal. This is reflected in the prompt disappearance of inorganic radioiodine from the blood stream and diminished urinary excretion of I-131. The drop in blood level of circulation I-131 caused by rapid absorption by the thyroid is short lived for within four to eight hours, and in some very severe cases one hour, the level of protein bound radioiodine starts to rise.

RADIOACTIVE IODINE IN DIAGNOSIS

Various aspects of the body's handling of I-131 have been studied in an effort to arrive at a simple and reliable test to establish the presence or absence of disease.

The urinary excretion of radioiodine subsequent to ingestion was the first method, and it is still widely used. The method is simple and has the advantage of requiring only two visits by the patient. A tracer dose of 40 to 100 microcuries of I-131 is given, and all urine for 24 or 48 hours is saved. The quantity of radioiodine excreted is compared to the quantity given and the ratio expressed as per cent (See Figure 2).

The rationale for the test is simple; the hyperactive gland takes up more I-131 than the normal, leaving less to appear in the urine.

Comparison of Per Cent Excretion of I-131 with Respect to Time in Various Thyroid States

Author	*Time*	*Normal*	*Hyper*	*Hypo*
Werner[34]	24	52	17	55
Spanse[35]	48	52-85	6-33	73-91
Orshy-Schmidt[36]	24	42-80	5-43	48-93
Pawson[37]	Total	80	16	..
Keating[38]	48	60-70	720	..
Soley[39]	24	53-81	..	91-94
Arnott[40]	48	52-62	11	91

Figure 2

The rate of excretion of radioiodine in the urine rather than the amount has been analyzed. This requires frequent specimens and numerous determinations so is not applicable as a clinical tool. The added information is of little if any help.

Direct measurement of the in vivo uptake of the given dose by the thyroid gland, using an externally placed counter, has been widely used, and many modifications have been suggested and investigated to increase the sensitivity and specificity of this method. The most common technique uses a G.M. tube, modified G.M. tube (gamma sensitized), a heavily shielded collinated scintillation counter, or scanner device.

The patient is given from 1 to 100 microcuries of I-131 orally, depending upon the sensitivity of the detector used. At 24 hours the amount of in vivo I-131 in the thyroid (total) is measured by placing the detector approximately 25 cm. from the isthmus of the thyroid. A thigh count is also made at this distance

and this activity subtracted from the total neck activity over thyroid to correct for background neck activity. This corrected neck activity is then compared to the activity of a 25 ml. I-131 standard containing 100 per cent of the dose given, measured at the same distance (25 cm.). The result of the corrected neck (thyroid) activity is then expressed in per cent of standard dose activity. Figure 3 shows the ranges reported by several investigators.

Through the use of highly sensitive gamma detectors (scintillation), doses as low as 0.2 microcuries have been used for accurate in vivo uptake measurements over thyroid. This offers the advantage of low dosages, thereby allowing repeat doses which are still within the tolerance range.

Comparison of Per Cent of 24-Hour Uptake of I-131 in Selected Thyroid States

Author	*Normal*			*Hyper*			*Hypo*		
	High	*Low*	*Av.*	*High*	*Low*	*Av.*	*High*	*Low*	*Av.*
Werner[41]	34	11	21	76	33	60	4	1	3
Hamilton[42] Soley	45	10	20	92	13	60	10	0	5
Freedgerg[43]	65*	14	28	97	42	64	..	..	14

* Only one above 41%, this in a non-toxic diffuse goiter.

Figure 3

Earlier reports of this method were not too satisfactory as several cases of obvious thyrotoxicosis had normal and even low uptakes. Several explanations may be offered in the light of our present knowledge. The workers used rather large doses of I-127 as carriers; we know this latter substance may alter the uptake of I-131 by competing for thyroid space.[35] Many patients had received iodides, or one of the goiterogenic drugs, or both, prior to study, and this markedly reduced I-131 uptake. A final possible source of error lies in the fact that small tracer doses, 15 to 150 microcuries, may reach their peak uptake in one to six hours in highly overactive glands and be in a large part excreted by the end of 24 hours. Measurement of the uptake at one, six and 24 hours has been advised to overcome the latter error.

In seeking to overcome the variables inherent in external counts, gland size, gland position, and thickness of the overlying tissues (scatter, geometry, and absorption), one group[43] used four and eight counters arranged in a circle with the patient placed in the center. Despite the authors' enthusiasm, critical analysis fails to reveal any advantage over the single tube or scintillation head measurement.

The rate of accumulation of iodine by the thyroid has been determined and the resulting gradient has been used to differentiate hyper- and hypofunction. This method, plotting the uptake against the square root of the time, offers no advantage over simple measurement of glandular uptake.[44]

Finally, the rate at which radioactive iodine is bound to protein has been studied. This test is based on the premise that protein bound iodine is hormonal iodine, and the thyrotoxic thyroid by definition puts out an increased amount of such iodine. This fact was noted in animal experiments repeatedly but was not mentioned in human studies until 1949.[45]

A unique blood conversion method,[46] presented in 1953, uses the determination of the red cell:plasma I-131 ratio for calculating the rate of formation of nondiffusible (organic) fraction of I-131 in plasma under varied thyroid states. Maximum differentiation of apparent hyperthyroid and euthyroid states was observed at 24 hours, whereas maximum differentiation between hypothyroid and euthyroid states was not observed until 72 hours following the ingestion of inorganic I-131.

This method is now used as a routine diagnostic procedure by employing the increased gamma sensitivity obtained with a well-crystal scintillation counter. With this high sensitivity, I-131 activity of cells and plasma can be followed for at least 72 hours following the ingestion of only 25 to 30 microcuries of inorganic I-131.

This method offers a greater degree of differentiation of thyroid states than either the in vivo uptake or urinary excretion methods.

An excellent series of cases studied diagnostically with I-131 was published in 1950 by Keating et al.[47] These authors employed seven methods in all cases and compared them. The observation consisted of:

1. *Urinary excretion:* the proportion of the tracer observed in the urine collected for 48 hours after administration.

2. *Renal fraction:* the fraction of the dose that would ultimately appear in the urine if the initial simple relationship obtained.

3. *Disappearance rate:* the proportional rate expressed as per cent of tracer dose per hour at which the ingested I-131 disappears from the blood.

4. *Renal excretion rate:* the rate expressed as per cent of tracer dose per hour at which I-131 appears in the urine.

5. *Extrarenal disposal rate:* the rate at which I-131 is being removed from the blood by all tissues other than the kidneys.

6. *Thyroidal accumulation:* the per cent of the tracer dose found in the thyroid by external count at 24 hours.

7. *Accumulation rate:* the proportional rate expressed as per cent of tracer per hour at which the thyroid accumulates the tracer.

After these exhaustive studies the authors concluded, "The striking feature about the four measures of radioiodine accumulation which we have compared

is the fact that they are all nearly equal to one another in diagnostic sensitivity." They pointed out that false positive thyroid accumulation and urinary excretion were seen in patients with impaired renal function and cardiac decompensation.

In summary then, any of several tests is satisfactory in determining the thyroid status with I-131. The normals vary slightly from laboratory to laboratory but are quite distinct from the findings in hyperthyroidism. There is less clear delineation in hypothyroidism, and frequently the I-131 study is inconclusive. The factors, other than thyroid dysfunction, which cause alterations in results that must be considered in every case are:

1. Ingestion of iodine in any form.
2. Ingestion of any goiterogenic drug.
   a. Sulfonamides
   b. Thiourea, thiouracil
   c. Cyantis
3. Ingestion of hormones.
   a. ACTH, cortisone
   b. Thyroid
4. Exposure to radiopaque material.
   a. Lipiodol-bronchoscopy
   b. Priodax-cholecystography
   c. Diodrast-pyelography
5. Cardiac decompensation.
6. Impaired renal function.
7. Addison's disease.

RADIOACTIVE IODINE IN THERAPY

The rationale of I-131 therapy is based on two well-established facts:

1. Radiation will destroy thyroid tissue and thereby reduce hormone output.

2. Radiation can be delivered quite selectively to the thyroid gland by I-131 due to the gland's affinity for iodine.

I-131 gives off two kinds of radiation, beta particles with maximum energy of 0.6 million electron volts and a maximum range of 2.5 mm. in tissue, and gamma rays with energies of 0.37 to 0.08 million electron volts and much greater range of penetration. The beta particles expend practically all their energy within the body of the gland and are actually the effective emissions because the more penetrating gamma rays pass out of the gland and cause practically no ionization.

The unit commonly used to express quantity of the isotope is millicurie, which is by definition the quantity undergoing 3.7×10^7 disintegrations per second. In order to establish a comparison between the radiation produced by x-ray and isotopes, the term "equivalent roentgen" has been introduced. This term applies to beta radiation only and represents that quantity of beta particles which under equilibrium conditions releases in one gram of air as much energy as one roentgen of gamma rays. Some idea of their relative size can be appreciated if one remembers complete disintegration of 1 millicurie of I-131 per gram tissue produces 160,000 equivalent roentgens. Dosage is usually expressed in terms of milli or microcuries, but a simple formula can be used to approximate the dosage delivered to the gland in equivalent roentgens (e.r.). This formula was derived from the original work of Marinelli et al.[48]

This allows one to compare the energy delivered to a tissue by the isotope to the energy delivered by a similar amount of x-ray, the biological effects of which are much better known.

The dose of I-131 needed to produce the desired changes within the thyroid depends on several factors.

The first is the size of the gland. This is most difficult to determine with any certainty. One experienced observer[49] who checked his impressions against the actual size of the gland as found at surgery, was unable to reduce his error to less than 25 per cent, so we may assume an error of 50 per cent would not be surprising in average hands. Distressing as such inexactitude may be to physicists and radiologists who have calculated the dosage in exact terms of microcuries per gram, as we will see later, clinical responses can be predicted quite accurately by simply calling the glands—not palpable, palpable, large, and extremely large.

The second factor is the effective half-life. This involves the actual per cent of the dose given that is taken up by the gland and the rate at which it is excreted by the gland. This can be determined by tracer dose prior to therapy, for the gland handles doses of from 10 to 25,000 microcuries very much the same in most cases.[50] When glandular size and effective half-life have been determined, one variable remains which defies estimation.

The sensitivity of the individual thyroid to radiation. This cannot be anticipated prior to treatment, and variations from the mean will lead to both over and under dosage. Delivery of 9000 e.r. to the diffuse hyperplastic gland is a generally accepted reference dose in diffuse glandular enlargement. This is the average x-ray dosage found to produce the de-

$$\text{dose, e.r.} = \frac{\text{microcuries given} \times \text{uptake \%}}{\text{weight of gland in grams}} \times \frac{\text{effective half-life (days)}}{8 \text{ half-life I-131 (days)}} \times 160$$

Formula I

sired therapeutic effect. Much greater doses are needed to affect nodular and normal glands.

Once the two measurable factors listed above have been determined, the required dose to deliver 9000 e.r. can be derived by rearranging Formula I.

While such calculations may give an air of scientific accuracy to the dosimetry in I-131 therapy, one should realize that any formula in which a major factor may err by 50 per cent cannot be taken too seriously. At present, certain clinics are using arbitrary doses which they prescribe as follows: not palpable, 2 millicuries; palpably enlarged, 5 millicuries; very large (two to three times normal), 10 and 15 millicuries. Only through such arbitrary means has the dosage required in toxic nodular goiter been arrived at.

$$\text{Treatment dose in microcuries of I-131} = 160 \text{ rep} \times \frac{9000r}{\frac{\text{Biol } \frac{1}{2} \text{ life (days)}}{\text{Physic. } \frac{1}{2} \text{ life—8 days}} \times \text{Max. uptake \%}} \times \text{Est. gram wt. gland}$$

Formula II

The determination of the dosage of I-131 needed to obliterate thyroid function is still only a quasi-quantitative procedure. Attempts to compute dosages on estimated thyroid weight and on measurements of uptake and disappearance rate of a previous tracer (test) dose have not been entirely successful. Due to slow depletion of thyroxine stores in the gland, a clinical evaluation of the effect of a therapeutic dose is subject to a delay of many weeks. A method for early estimation of the effect of thyroid function would save months of time in the clinical management of the patient. The identification of the iodinated components of plasma by paper chromatography led certain authors to conceive the idea that alterations of these components during I-131 therapy might be valuable in predicting therapeutic results.

These investigators[15] used filter paper chromatographs made of the blood plasma of 19 hyperthyroid patients and four patients with intractable angina pectoris. Plasma radioautographs show correlation as follows: disappearance of the thyroxine band, usually between two to seven days, forecasts clinical hypothyroidism; reduced intensity of the band during this same interval forecasts euthyroidism.

This suggests that chromatographic plasma analysis may provide the means for obtaining closer control of I-131 therapy of the thyroid. Within two to seven days, the evidence obtained appears to indicate that one can predict the therapeutic result which clinically is not evident for one to five months because of the slow depletion of thyroxine stores in the gland.

RESULTS OF RADIOACTIVE IODINE THERAPY

Whether the rationale of I-131 therapy is sound or faulty is unimportant; the results obtained by such therapy are the criterion by which the method must be judged. Now, 13 years after the first trial of I-131, enough data has been compiled to make it possible to reach some conclusions concerning its efficacy. The general results of several of the larger series reported to date are contained in Figure 4 and will be discussed later. Brief analysis of the series arranged in chronological order shows a gradual improvement in results and a simplification of methods.

Hertz and Roberts [51] reported in 1946 on 29 cases treated from 1941 to 1946. Their data are hard to evaluate for they used a mixture of I-130, 90 per cent and I-131, 10 per cent. This makes comparison of dosage impossible, for the 12.5-hour half-life of I-130 gives a biological half-life very different from that of the 8-day isotope, I-131. Their high failure rate, 9 in 29, may have resulted from too prompt institution of iodine therapy following the administration of the radioiodine, for we know that large doses of stable iodine have the property of washing out radioiodine if given within 72 hours.

The same I-130 and I-131 mixture was used by Chapman and Evans [52] on 22 patients treated from 1943 to 1945. These workers used considerably larger doses and by so doing were able to cure hyperthyroidism in 20 of their 22 cases. However, six of their patients noted mild reactions resembling radiation sickness, and four of those cured of thyrotoxicosis developed myxedema requiring thyroid therapy.

In a later series of 48 cases treated with I-131, Chapman obtained cures in 36 on a single dose and improvement in 12. The author used the status six months following a single dose as his criterion for cure or improvement.

Soley and Miller[49] reported their results on 33 cases which were treated with 1,000 to 2,000 microcuries of I-131 every month until a therapeutic response resulted. Twenty responded well, becoming euthyroid in one and one-half to six months; doses ranged from 800 to 4,500 microcuries, averaging 2,726. The 13 failures were in the patients who had the largest glands and highest basal metabolism rates. When this series was extended to 61 cases and the initial dose increased in keeping with gland size and uptake, the failure rate fell from 33 per cent to 16

per cent. These 16 per cent were all improved but not euthyroid; hypothyroidism and myxedema occurred in 5 per cent.

Haines and Keating[47] attempted to give an initial satisfactory dose by administering 200 to 250 microcuries of effective I-131 per gram of thyroid tissue. Of 40 such cases, 27 had good results, 8 fair, and 5 poor following a single oral dose ranging from 2,600 to 20,000 microcuries. A second dose given to the 8 fair cases resulted in raising the total of successes to 35. This series was made up of complicated cases, and the five failures were in patients with cardiac decompensation and renal insufficiency which may have led to erroneous diagnosis.

Williams[53] treated 98 unselected cases of thyrotoxicosis with I-131, attempting to give a satisfactory initial dose. Follow-up on 80 of these in 1948 revealed no failures; 76 of the patients had been euthyroid for from 4 to 12 months. The remaining four were myxedematous. This gives the amazing result of 95 per cent cure!

Printzmetal[54] used the 8-day isotope to treat 18 patients in whom surgery was contraindicated because of multiple recurrences, heart failure, emotional lability, or extreme toxicity not amenable to thiouracil. Sixteen were rendered euthyroid, one improved, and one was a frank failure. The failure occurred in a *toxic adenoma.* The total dose was 11 millicuries. In the light of Crile's report, vide infra, this patient received an inadequate dose.

In a series of 26 uncomplicated cases, the same author reported good results in 25 with improvement in the other case. However, in this series the occurrence of hypothyroidism was 15 per cent.

Very little differentiation between diffuse toxic goiter and nodular toxic goiter with reference to dosimetry was made prior to Crile's[55] excellent report. Crile reported the only fairly large series of toxic nodular goiters treated with I-131. The 37 patients were selected by the following criteria: all were 40 or older; solitary adenomas were not treated; any case showing recent growth or in which the character of the nodules suggested malignancy was excluded. The dosage was arrived at by trial and error as the formulas used in diffuse toxic glands failed to apply to this group. As will be seen in Figure 5, the total dose needed to effect remission correlated roughly with gland size.

Comparison of Results of I-131 Therapy following Varied Doses of Radioiodine

	Chapman	*Soley Miller*	*Hains Keating*	*Crile*		*Printzmetal*		*Moe*		*Williams*	*Total*
				Diff	*Nod*	*Comp.*	*Uncomp.*	*Diff*	*Nod*		
Number	65	61	40	12	37	18	26	67	33	80	439
Range of I-131 Microcuries	10000	3060 7556	—	7200	11000 77000	5320	4400	1100 17800	1200 43900	—	—
Time till normal months	2	3.2 13.4	2.6	4	5	4	3	3	—	—	—
Hypothyroid & Myxedematous	6%	5%	17%	8%	0	0	15%	15%	6%	5%	8%
Cure of hyperthyroidism: Good	86%	84%	67%	91%	86%	89%	96%	85%	94%	95%	91%
Fair	12%	16%	20%	9%		11%	4%				6%
Poor	2%		13%		14%						3%

Figure 4

Class	*Size*	*Total Dose (in Millicuries) Needed to Cause Remission*
Class 1	less than 50 gm.	23.4
Class 2	50-100	30.6
Class 3	100-150	37.6
Class 4	More than 150	66.2

Figure 5

Initial doses ranged from 7 to 15 in Class 1 to 17 to 28 in Class 4. This amount is much more than needed in the diffuse gland; however, the author states that he now uses an initial dose of from 17 to 21 millicuries routinely regardless of gland size. This regimen induced remission in 32 of the 37 cases. No myxedema was seen. The five cases not in remission by the end of six months received total doses of 27 to 77 millicuries. The author concluded that most cases of toxic nodular goiter can be controlled by I-131 and that in cases where surgery is not feasible it is the treatment of choice.

In September 1950, Moe[56] reported on 100 cases, 67 diffuse and 33 nodular, that were treated with an initial dose of 100 millicuries I-131 per gram of tissue as calculated by Formula II. The patients were

seen in two months when further therapy was decided upon as follows: no improvement, repeat the initial dose; marked improvement, give no further I-131. The degree of improvement between these two extremes was estimated by the usual clinical means, and a proportional dose of the intial dose was given, i.e., a patient improved by half would receive half the initial dose. This method gave 88 per cent cures, 9 per cent hypothyroidism, and 3 per cent myxedema. It is interesting to note that doses used in nodular glands were larger than the diffuse and the occurrence of hypothyroidism much less, 6 per cent to 15 per cent.

An over-all statistical analysis of the 439 cases listed in Figure 4 gives the following results, if only abolition of hyperthyroid is considered:

Good—91 per cent
Fair — 6 per cent
Poor — 3 per cent

The incidence of hypothyroidism and myxedema has to be taken as a group for most authors did not separate these conditions. There were 34 cases reported as needing thyroid therapy, an incidence of 8 per cent.

COMPARISON OF RADIOACTIVE IODINE WITH OTHER MEANS OF TREATMENT

At present there are three methods other than I-131 which can be considered in the treatment of hyperthyroidism. A comparison of these methods with radioiodine therapy will point out the advantages of each.

1. *External radiation.* Application of radiation to the thyroid by x-ray or radium collar has been used very little in recent years. Results from different series varied greatly. Groover and Christie[57] reported on 252 cases treated by x-ray. They administered 200 r to 3 parts every 3 weeks until a satisfactory result ensued. They report: 80 per cent cured; 15 per cent improved; 5 per cent failures. Among their successes, one-third were cured within 18 weeks; one-third in from 18 to 30 weeks, and one-third by the end of 30 weeks.

On the other hand, Means,[58] in summarizing all the cases treated by x-ray at Massachusetts General Hospital, felt that one-third were cured, one-third were improved, and one-third resulted in failure. In either case this method does not compare to I-131 in results, simplicity, cost, nor speed, and it retains the drawback of I-131, namely possible cancerogenic properties.

2. *Propylthiouracil.* This drug is named specifically, for it is the most effective and least toxic of the thiouracil group of drugs now available. A huge volume of literature has accumulated concerning the drug, the consensus of which expresses the following general ideas:

Control of hyperthyroidism can be achieved in 98 per cent of patients who can tolerate the drug in doses of 150 to 600 mg. a day.

Remissions of long duration will result in from 0 per cent to 85 per cent after several months of continuous adequate therapy (50 per cent probably is about right.)

Toxic reactions occur in about 15 per cent of all cases; however, less than 1 per cent will be severe enough to force discontinuation of therapy.

The disadvantages of the drug are the necessity of frequent blood counts and protracted medical supervision. Mortality directly attributable to the drug is 0.5 per cent.

3. *Surgery.* Certainly surgical treatment of diseases of the thyroid is one of medicine's true triumphs. The results of subtotal or total thyroidectomy in treatment of hyperthyroidism show marked uniformity from one group to another.

Cole,[59] in reporting the series at the University of Illinois Research and Education Hospital, noted a mortality of 0.61 per cent in 487 cases of diffuse goiter and 1.58 per cent in 315 cases of toxic nodular goiter. He made no mention of the occurrence of postoperative hypothyroidism but did mention an instance of 1.5 per cent vocal chord palsies.

Cattel[60] reported an operative mortality of 0.24 per cent in 1,630 consecutive patients operated upon for hyperthyroidism at the Lahey Clinic. He noted hypothyroidism in 4.5 per cent of this series and recurrence in 2.4 per cent.

Drawing from these two series, both large and representing the best results that can be expected, one gets the feeling that surgery is safe, uncomplicated, has no failures and few, if any, poor results. However, before accepting these results, accurate as they may be, the results obtained at the University of California Hospital[61] should be mentioned. It may or may not be significant that follow-up on this group was not purely a function of the surgical staff but was a cooperative effort of the medical, surgical, opthalmological, and radiological departments.

One immediately notices that the incidence of postoperative hypothyroidism is about four times that noted in other series. In other respects the results are comparable with those of the Chicago and Boston groups. In general then, we can summarize surgical therapy by saying: In well trained hands there will be 3 per cent failures; that is 0.5 per cent to 1 per cent deaths and 2 per cent to 2.5 per cent recurrences. Unsatisfactory results will occur in an additional 2.5 per cent, 1 per cent from recurrent laryngeal nerve paralysis and 1.5 per cent from postoperative tetany. Therefore, it seems that 95 per cent good results can be anticipated.

Complication	*379 Diffuse Toxic*	*179 Nodular Toxic*
Hypothyroidism	20 %	21 %
Myxedema	9.2%	5.5%
Recurrence	3.6%	0.5%
Hypoparathyroidism	1.5%	0.5%
Vocal cord paresis	3.3%	4 %
Vocal cord paralysis	2.1%	3.1%
Mortality	1 %	0.5%

As one compares the methods of therapy, several facts seem apparent. External radiation offers no advantage over isotope therapy and will probably continue to decrease in usefulness.

Thiouracil drugs offer slightly more rapid return to normal than I-131 alone, but the added expense of frequent blood studies and follow-up visits as well as the high incidence of troublesome toxic reactions makes these drugs onerous to both patient and physician.

Surgery offers a cure rate of 97 per cent as opposed to 91 per cent in therapy with I-131. However, surgery has a definite mortality, a definite incidence of tetany, and recurrent nerve paralysis which total from 3.5 per cent to 4 per cent irreparable bad results never seen with radioactive iodine. The incidence of hypothyroidism of 8.5 per cent for I-131, and from 5 per cent to 20 per cent for surgery, is probably nearly equal.

Two objections to I-131 are frequently raised by those who advocate surgical therapy. The first is longer morbidity in isotope therapy. However, let us analyze two situations and compare them.

Severe thyrotoxicosis, surgical therapy: preoperative preparation with thiouracil and iodine—roughly one day for every one per cent elevation in basal metabolism rate; average 57 days in Lahey's series.[62] Postoperative hospitalization, 7 to 10 days; total days in hospital, 64 to 67.

Severe thyrotoxicosis, I-131 therapy: tracer study, one day; administration of therapeutic dose of I-131, one day; three day delay. Thiouracil and iodine given after treatment to induce remission equivalent to that prior to surgery—57 days. Total time in hospital—62 days.

Mild thyrotoxicosis, surgical therapy: 10 to 14 days Lugol's therapy prior to hospitalization; operation 3 to 5 days postoperative hospital stay; total hospital stay, 3 to 5 days.

Mild thyrotoxicosis, I-131 therapy: tracer dose, out patient; treatment dose, out patient; Lugol's started 3 days after I-131 treatment; total hospital stay—0.

In general it is safe to say that regardless of the degree of toxicity, a patient can be restored to health and activity by judicious use of I-131 followed by iodine as rapidly as by surgery.

The second objection to I-131 is its possible cancerogenic properties. The answer to this no one can predict; however, some idea can be obtained by observations on the late effect of x-ray on thyroid tissue. A survey[63] was conducted in which questionnaires were sent to 70 radiologists and 31 thyroid specialists in which these questions were asked:

1. Have you ever seen cancer arise in a thyroid gland treated by x-ray for hyperthyroidism? Was it nodular?

2. Have you seen cancer arise in adjacent structures?

3. Have you seen cancer arise in normal thyroid which was radiated because it fell in the field of adjacent malignancy?

4. Have you seen cancer arise in thyroid glands treated by means other than radiation?

Ten cases fitting question one were reported; but by analysis, only three could be considered since the time interval was too brief in the rest.

In response to question number two, eight cases of cancer of the skin due to radiation were reported, two cancers of the larynx occurred, and one each of the esophagus and trachea. The incidence of these conditions to that of the general population was not compared.

In answer to question three, no one reported having seen cancer arise in normal thyroid, though many radiologists said they must have given much larger doses in treating laryngeal carcinoma than was ever used in therapy of hyperthyroidism. Follow-up of many cases was over 10 years.

Nine cases of cancer arising in thyroid glands treated surgically were reported. While many were stated to be nodular goiters, two were reported specifically as diffuse toxic goiters.

The authors conclude the possibility of late malignant degeneration following radiation is negligible, and it may be presumed it is not appreciably greater in radioactive iodine therapy.

In summary, then, morbidity is the same in both methods, the cure rate is slightly higher in surgery; however, surgery has about 3 per cent irreparable complications never seen with I-131. Against a possible carcinogenic factor in I-131, which has not been established, one must weigh the irreducible 0.2 per cent to 1 per cent mortality of any surgical procedure. The occurrence of post treatment hypothyroidism is probably the same in both methods.

AC

(you probably know every answer!)

Q. Which is today's most widely prescribed broad-spectrum antibiotic?

A. ACHROMYCIN — it's first by many thousands of prescriptions.

Q. What are some of the advantages of ACHROMYCIN?

A. Wide spectrum of effectiveness.
Rapid diffusion and penetration.
Negligible side effects.

Q. Exactly how broad is the spectrum of ACHROMYCIN?

A. It has proved effective against a wide variety of infections, caused by Gram-positive and Gram-negative bacteria, rickettsia, and certain viruses and protozoa.

Q. In what way are ACHROMYCIN Capsules advantageous?

A. For rapid and complete absorption they are dry-filled, sealed capsules (a Lederle exclusive!) No oils, no paste...tamperproof.

Q. Who makes ACHROMYCIN?

A. It is produced — every gram — under rigid quality control in Lederle's own laboratories and is available only under the Lederle label.

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Recent reports concerning functional and histologic effects of therapeutic doses of I-131 on the thyroid gland of man have been reported by two groups of investigators. The first group[64] reported results on 29 cases in which evaluations were made between two days and eight years following administration of I-131. Results are as follows:

1. Difficulties were encountered in separating lesions due to radiation from those occurring from other causes.

2. Oral doses below 7 millicuries produced changes which were not recognized as due to radiation.

3. Oral doses 15 millicuries and above showed changes which were consistent with radiation effects (severe fibrosis).

4. Frequent findings were those of bizarre hyperchromatic thyroid epithelial cells regarded as exhausted or over stimulated non-functioning thyroid cells. These observations were found as frequently in non-irradiated thyroid glands with disease processes.

The results of the second group of investigators[65] on 23 patients with hyperthyroidism are as follows:

1. Twenty-one out of 23 became euthyroid following I-131 therapy.

2. Seven patients had glands which were predominantly hyperplastic with no definite radiation effects noted.

3. Nine patients had lesions identical with those of Hashimoto thyroiditis. This represents one effect of internal radiation with I-131.

4. Four glands contained multinodules and showed moderate follicular atrophy of the residual glandular tissue as a result of injury by ionizing radiation.

5. Three glands showed diffuse follicular atrophy with extensive fibrosis regarded as classical lesions of I-131 therapy.

6. Vascular disease in three glands was minimal and had no relation to the regressive thyroid lesions observed.

The results of these investigations present the difficulties involved in an attempt to verify or rule out the cancerogenic factor in I-131 radiation on a histological basis at this time.

SUMMARY AND CONCLUSIONS

1. Radioactive iodine is a highly sensitive tool for the study of various thyroid states and of over-all body iodine metabolism.

2. Radioactive iodine is the therapy of choice in any case of hyperthyroidism in which surgery is contraindicated.

3. If 100 microcuries of radioiodine per gram of thyroid tissue is given in cases of diffuse toxic goiter, 75 per cent of all treated cases will be made euthyroid. Second or third doses will give 91 per cent cures, 6 per cent improved, and 3 per cent failures. The above results indicate that a more effective means of controlling therapy is desired. This can be obtained by employing a paper chromatographic method which is based on the initial changes in the iodinated plasma components which have been correlated with the clinical course in previously treated cases.

4. The amount of I-131 required to bring about remission in cases of toxic nodular goiter is much greater than in diffuse toxic goiter. There is also some question as to whether toxic nodular goiter should be treated with I-131 due to the incidence of malignancy associated with nodular thyroids. It seems logical that one should not treat a gland with I-131 in which its pathology is uncertain. The only treatment in this case should be surgical, especially when there is a possibility of malignancy.

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We will endure . . . if we accept our obligation to maintain stability in our world by conserving the traditions and institutions of the past and encouraging the orderly forces of progress. Those of us who assume that the capitalist society can and must endure rally around these standards. We believe in property but know it can flourish only when innovation has free rein and new enterprises (with the personal rewards that must go with them) can emerge. We are devoted to the idea of equality . . . of opportunity to rise. We are committed to the idea of man's rationality and his ability to make free choices for his own betterment and that of society.

—*Louis M. Hacker*

A Medical Student Looks at Blue Shield

William Kent Murphy

Galveston, Texas

To me, as a medical student, the problems to be faced as a practitioner are not immediate ones—but they will be! Coming, as I do, from a home of moderate circumstances, the expenses of medical care are of paramount importance to me as a matter of principle and to myself and my future patients as a matter of economics.

It is with this in mind that I take a look at Blue Shield and what it represents to me and my patients-to-be. I have often pondered the problem of medical economics, and before I understood more about the subject, I was quite a heretic from the standpoint of the medical profession. I could not see any solution to the burden of medical finances except Federal Compulsory Health Insurance!

For a moment, let us look at these expenses through the eyes of a person of low income. Let us consider what, to my family, and even more so to families of really low income, is the overwhelming problem of medical economics. People who have been reduced to poor circumstances are there often as a result of sickness and accidents. To people who have no "margin" to take care of medical bills, prolonged sickness looms as one of the most dreaded eventualities which can occur. As a result, they often ignore the obvious danger signals of insidious and crippling illnesses in the hope that such symptoms will "go away"!

If the breadwinner of a family, who can barely make ends meet, is stricken with illness, the tragedy is multiplied. It does not take a long illness for the head of a household to find himself permanently behind the eight-ball financially. Medicine is expensive, hospital care higher, and in addition there is the expense for the doctor without whom the other expenses would be futile. Operations, prolonged bed rest, expensive treatment by specialists, all the marks of adequate medical care, can represent to the person of moderate income a tremendous obstacle. Since bad things seem to come in three's, physical recovery for the wage-earner may mean nothing but a return to work for years to pay for bills of his sickness and that of his family.

To me, as a person who has seen some of the results of such bouts of illness, as who of us has not, the problem is in sharp focus. Maybe this among the many challenges of medical practice rates as one of the primary reasons for my coming to medical school —to be of genuine help to people in their illness. This was the reasoning by which I considered federal health aid a necessity to the welfare of the many. It does not take long, however, to realize that good intentions do not remedy bad situations.

As a medical student, it is not hard for me to see why doctors violently oppose federal intervention in medicine, and as an American, I can feel the pride of my chosen profession in its achievements and progress, the vital enemy of which is regimentation under any guise.

What then of the welfare of the masses of people to whom medical care can be a tremendous burden? I shall not say that the answer has been found completely, but there is at least hope for a future, free from federal control, when doctors will be free to help people in their sickness and trouble without their services becoming a financial burden to their patients.

What is this glimmer of hope? It is the cooperative spirit and farsightedness of a few of the medical leaders who, as long ago as 1939, envisioned a voluntary health insurance program. At that time the medical profession began to work out its answer in a concrete way to the problem of the expensiveness of medical and surgical care—Blue Shield.

A discriminating person will not accept what he hears and reads at face value, but will delve into things that interest him with an eye toward discovering the values and defects of those certain things. An evaluation of Blue Shield is no exception. Insurance is no new thing in the field of American business, so why should "another insurance plan" seem to light a path to future health for the people? What is it in Blue Shield that is particularly of interest to both the medical practitioner and to the public?

It is not the purpose of this discussion to go into the theory of insurance, nor to repeat what booklets long since prepared say much better. As a person who has just begun to explore this field, I would like to point out what I consider to be the important features of the Blue Shield Plan.

Let us look at it first from the standpoint of a young and eager doctor, to whom the welfare of his patients is of paramount importance. To such a person, high charges on the part of a doctor for medical care, when applied to people of low income, seem incongruous, and they are! Medical care, however, is expensive, and for that there is no cure. If then,

This essay won third prize in a national contest sponsored by Blue Shield and the Student American Medical Association. Mr. Murphy is a student at the University of Texas School of Medicine.

there were some plan of paying for care during sickness before it is necessary—!

We are all familiar with commercial health insurance. I am sure more than a few people have felt the sting of a misplaced confidence in such insurance. This is not to say, however, that there are not good insurance policies of the commercial variety, because there definitely are.

Blue Shield represents, on the other hand, a plan which can well merit the confidence of its purchasers. No plan for helping alleviate the ticklish problem of medical economics could survive without the help of both the medical profession and the people as a whole. Blue Shield represents a start toward the goal of affording to people the benefits of prepaid insurance against medical bills. More than that, it represents the beginning of an intelligent response on the part of physicians toward the problem that threatens their existence as a free system under the American tradition of free enterprise.

No one can understand medicine better than those people who make up the nucleus of medical science, the physicians in practice. It is only logical, then, that they be the ones who institute a method for voluntary health insurance. Not only that, but it is their responsibility to see that efforts are made on the part of the profession to cut down overcharging and excess extra fees. What better assurance against this is there than a plan whereby doctors cooperate to help cut medical costs! In this respect Blue Shield represents a step in the direction of correcting some of the problems intraprofessionally, as well as those with the general public.

Another important point in favor of Blue Shield is the fact that it is a non-profit organization. Most insurance companies are run for a profit, which is logical enough. It is well known, however, that the "middle man" often raises costs greatly. In the Blue Shield plan for pre-insurance, the method for allaying some of the costs of medical expenses does away with a profit-making intermediary, something which potentially could lower costs of medical insurance greatly. This is not to say that commercial insurance is taboo, but for people who can barely afford any insurance, one which deals directly with the source of expenses is far more economical than an indirect dealing. Blue Shield does, in effect, eliminate the expense of a middle-man, since it is a non-profit organization.

Among the other important points to be considered in setting up an idealized system for medical and surgical insurance is that of adaptability of a plan to local needs. Here again Blue Shield has the edge on nationally run plans in that individual plans are set up by doctors in the areas to be served and can be tailored more or less to fit the economic status of the section involved.

To turn the mirror around, let us look at the benefits to be derived from Blue Shield by the people for whom it is intended. To begin with, the original plans were set up to cater to people of low income brackets; they were set up to make some type of health insurance available to the people which would give them real benefit without "skinning" them in the process. Blue Shield represents a concrete means of paying the doctor as the grocer is paid, day to day and week to week. Thus medical and surgical bills may be defrayed before they are incurred, and in small amounts.

Blue Shield offers to the people a plan backed by the people who are going to be most concerned with it, other than the sick patient, namely the doctor. This plan is a dependable plan and can be entered into at low cost, relatively speaking, without the fear that the insurance thus bought will be useless when it is needed, as is so often the case with insurance not backed by so reputable an organization as the American Medical Association.

All this seems far afield from the theme of this paper, but it represents concretely the view of one medical student as he looks at Blue Shield. Anyone who looks at an item looks at all of it before he passes judgment on it. Therefore, I have tried to look at Blue Shield from my former standpoint, my present position, and my future point of view.

Blue Shield represents to me a plan which, if my patients possess it, will enable me to give them the kind of care they need physically without defeating my purpose by burdening them with health-breaking bills. It is well known that part of treating illness involves the culture of a good psychological state of mind. It is hard to see how such a state could be obtained if the patient were constantly worrying (for good reason) about finances.

Blue Shield represents also the seed from which can grow the plan whereby the American medical profession can save itself from the often seemingly inevitable folly of national regimentation. Anyone who has been subjected to an indifferent health service knows that the best care comes, not from those who are forced to serve you, but from those whom you choose to serve you! There is no inspiration to a person greater than that of the confidence of his fellowman. Blue Shield allows patients free choice of doctors and at the same time does not attempt to set fees or place undue restraint upon the doctor. It does, however, place a certain moral obligation upon the doctor to be fair. Thus when a patient chooses a physician and places in him his confidence, that physician is bound by all that he is to try to merit that confidence.

No discussion is complete without criticism. Thus it is necessary to point out problems and weaknesses, as I see them, which appear in a plan such as Blue

Shield. To begin with, this plan must be supported wholeheartedly by the medical profession if it is to survive. Half-way support just will not do the trick! When specialization is the order of the day in the medical field, and when fees skyrocket, only an alert profession can save itself from serious trouble. A doctor cannot forget the economic effects of sickness and disability upon his patients.

It is impossible for me to envision a profession dedicated to the physical welfare of mankind only, one which tries to isolate the physical being from the economic and psychological being. The man a doctor treats is "whole" and is not composed of disarticulated parts to be treated individually without regard to the whole. Blue Shield then represents a concrete beginning for keeping man economically well through sickness and health, but it is only a beginning. This plan must grow and be revised continually as dictated by experience and intelligent consideration.

The ideals of preventive medicine and high public health standards cannot be realized as long as people are unable to pay for preventive and diagnostic measures. Cancer, as an example, will never be controlled as long as diagnosis is as tedious and expensive as it is. Here the genius of medical science will help solve the problem, but no pre-insurance plan should be considered complete as long as it leaves untouched these problems which are pertinent to the health and welfare of the people. Wise heads say diagnostic and preventive measures cannot fall within the realm of pre-insurance, such measures not being financially feasible. This position must be re-examined thoroughly before such a conclusion is taken as final.

Blue Shield is obviously alive and awake to the problems to be faced before the enigma of medical economics is solved. The recent addition of "catastrophe" insurance is definitely a step in the right direction. No problem is greater than that of prolonged illness which requires expensive medical and surgical care as well as rehabilitation measures. As a medical student looks at Blue Shield, he sees plainly the challenge before him. Wise heads preceding him have given genesis to this plan which promises to be medicine's answer to health insurance.

The public, however, will continue to clamor for health insurance as long as it does not see or know about that which is plainly available to it. It is up to the doctor and to the prospective doctor to become acquainted with and acquaint others with the possibilities of Blue Shield. In the medical students of today are the minds which will give birth to the ideas for the future course of Blue Shield. Until it has fulfilled the need for public health insurance, Blue Shield will need revision.

It is worth the time of every medical student to acquaint himself with this plan before he is faced with the actual necessity of utilizing it in practice to the best advantage of his patient. As this medical student looks at Blue Shield, he feels the conviction that it represents a concrete beginning of the solution to the problems of national regimentation of the medical profession and of medical economics.

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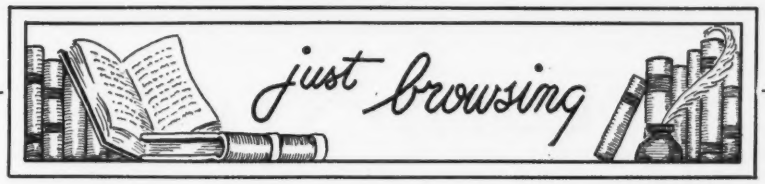
Aside from diagnostic ability and essential kindness, there is probably no quality in a physician for which patients are so grateful as the ability and desire to explain, to answer their anxious questions fully and truthfully, to be as frank as knowledge will permit. From personal experience I know what unhappiness can result from failure to explain; I know also that few things in medical practice bring such deep satisfaction to doctor and patient as frankness.

H. M. Marvin, President
Connecticut State Medical Society



Every former student of Dr. Ernest Sachs invariably has most vivid recollections of his "Thursday Clinics," remembering them as terrifying experiences at the time (especially if he was "in the pit"), yet the source of facts, principles, and examination techniques which have never been forgotten since that memorable day of his junior year in medical school. In answer to numerous requests, Dr. Sachs recently published a group of his essays in a small book.* They make interesting and instructive reading, and will be of particular interest to those who attended his "Thursday Clinics" for a year. Some excerpts from "The Case That Has Been Unrecognized and Is Diagnosed Too Late" are characteristic.

"All of us have seen cases that have been unrecognized and in which the diagnosis has been made too late to help. This is one of the most trying experiences that a physician has to encounter. Probably no one ever handled such a situation with greater tact than William Osler, and he undoubtedly came across such instances innumerable times, for doctors and laymen from all over the United States consulted him when all else had failed.

"What should be the attitude of the physician towards his colleague when this happens? . . . Criticism of our colleagues accomplishes nothing and creates only hard feelings. We must exercise tolerance and keep in mind always that none of us is infallible, and that some of us have had greater advantages than others. These unfortunate occurrences can be obviated in the future only by proper instruction. It devolves upon every one of us who has had these advantages to give our less fortunate colleagues the benefit of our experience. The first requirement is to insist on a careful study of every patient. In the vast majority of instances, a detailed history and physical examination, carried out by a thoughtful physician, will give him a clue to his patient's trouble.

"Errors in diagnosis are most likely to occur in diseases that have an insidious onset and in which the patient's initial symptoms are vague and indefinite. Frequently, such patients do not receive the careful attention they deserve, and the diagnosis is missed because a thorough, complete examination has not been made.

"Every patient who comes to a physician, irrespective of how trivial his symptoms seem to be, should have a careful history and a complete physical examination. This seems obvious, but we all recall instances in which obvious points in examination have been overlooked or disregarded. . . ."

"All medical teachers should impress upon their students that they should never be too proud to call for help. The time has passed when one man can hope to know every phase of medicine. He should be frank to recognize this fact and not hesitate to tell the patient that another doctor can handle this particular problem better. There was a time, not so long ago, when in some communities it was considered a disgrace and reflection on a physician's ability if he asked for a consultation. Fortunately, that time has passed, and I doubt if there is any town or village today where the necessity and wisdom of a consultation is not recognized.

"A grave responsibility, however, rests upon the consultant because his attitude towards his colleague, while it might be of great help, could also do untold harm. If he does not handle the situation tactfully, he may harm not only himself but, far more important, create a distrust of his colleague which could ruin his practice. Especially where there are very few physicians in the community, it may cause much unnecessary unhappiness. Tolerance and consideration on the part of the consultant should always be his guiding principles."—*(O.R.C.)*

* Reprinted from *Pre-requisites of Good Teaching and Other Essays* by Ernest Sachs, The Shoe String Press, 51 Caroline Street, Hamden, Connecticut, 1954, by permission of the publishers.

PRESIDENT'S PAGE

DEAR DOCTOR:

The marathon endurance test is on. Since my last letter to you, I have done my best to represent you at the following meetings: the Pediatrics Training Program Panel at the medical center in Kansas City, the School Health Postgraduate Panel at K.U.M.C., Kansas City, the Kansas Trudeau Society and Kansas Tuberculosis and Health Association meeting in Topeka, the meeting of the Council of the Kansas Medical Society, the Kansas University Alumni Association annual meeting in Kansas City, the Golden Belt Medical Society gathering at Concordia, the annual meeting of the Menninger Foundation in Topeka, and the Northwest Kansas Medical Society meeting at Colby.

Our Oliver Ebel, executive secretary, is now out of his cast for a fractured fibula and is making a good recovery from a cholecystectomy. He is back on the job in full strength. Our executive assistant, Rueben Dalbec, did a yeoman's job during Oliver's illness. He deserves much vitamin P for his efforts. Vitamin P is the *praise* vitamin. Let us not forget to administer this P vitamin often and repeatedly, not only in our practice but also in our associations with the allied professions.

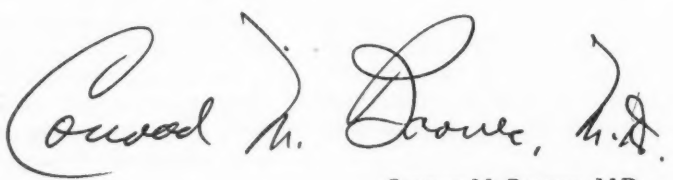
One of our big and important "hurdles" this year is the $25,000 we Kansas physicians need to contribute to the A.M.E.F. We do not desire more socialization and federal aid. Therefore, we must do our part to help raise the $10,000,000 needed to maintain the present high standards of our medical schools in this country.

Dr. Cyril V. Black, chairman of our Committee on Endowment, tells me that each Kansas physician must contribute at least $15 or more in order for us to meet our quota. All such contributions to the A.M.E.F. are tax deductible. Remember to send "In Memoriam" contributions to the A.M.E.F. instead of, or in addition to, flowers for the funerals of friends and departed loved ones. In spite of the fact that we have the largest medical school in the world here in Kansas, we Kansas physicians carelessly neglected to contribute our share to the A.M.E.F. last year. Let us do better this year!

All contributions to the John Porter Memorial Fund will receive credit in the A.M.E.F. and will, at the same time, maintain their identity in the John Porter Memorial Fund. This would be an excellent time to make your contribution! Ask your Councilor for further details as he will have a special doctor appointee in each county for the collection of A.M.E.F. contributions this year. I hope to be able to report on the progress of the Porter Memorial Fund when next I write.

In closing my letter for this month, I'd like to ask a favor of you. Please be a one-man public relations committee for doctors of medicine as you practice our science and art. You are proud of that M.D. degree. "Win Friends and Influence People" in its name . . . and remember about vitamin P!

Sincerely, in the Practice of the Art,



CONRAD M. BARNES, M.D.

EDITORIAL COMMENT

Federal Legislation

The A.M.A. Committee on Legislation held a regional legislative conference in Omaha on October 15, 1955. Representatives of 11 midwestern states were present, including several Kansas doctors.

Those who were at Omaha can see the need for a united effort on the part of the medical profession if medicine is to continue without federal assistance and ultimate complete federal control.

During the 83rd Congress some 300 bills directly affecting the practice of medicine were introduced. All but two of the United States senators signed their names to one or more of these health measures. This is pointed out to emphasize the popularity of health programs at the federal level and the weakening of public opinion in regard to a federal health program. Aside from this, it points to even more drastic action by Congress in the 84th session because of the election year.

The President's health reinsurance program which was defeated during the last session will undoubtedly be re-introduced. We will once again rely on the Democrats to defeat this measure. Even here one wonders if the vote is one of principle and understanding of the bill or the customary "No" vote on administration policy. Help from the Republican Party was and is needed, but it is interesting to note the party which defeated the bill during the last session.

It is most difficult to see who could benefit by health reinsurance. The insurance companies say there is little demand and believe there would not be much usage of such moneys. Private insurance companies have made incomparable strides during the past several years in bringing health insurance to the people. This bill is not designed to help those who do not have insurance, so its intent is not clearly understood by anyone. Yet medicine can look forward to a great deal of effort upon the part of the administration for the passage of this $25 million reinsurance bill in 1956.

The A.M.A. policy on veterans' affairs remains unchanged. The A.M.A. favors and actively supports legislation whereby the federal government provides care for these veterans whose disability was service connected or aggravated. On the other hand, they strenuously object to medical care provided for the veteran with no service connected disability. Yet in spite of A.M.A. objections, more than 1,000,000 additional veterans are becoming eligible for free medical care each year, and 85 per cent of those in veterans' hospitals in 1954 were veterans with non-service connected disabilities.

More than 30 separate bills on polio vaccine were introduced within a three-month period after the announcement from Ann Arbor revealing the success of the initial mass immunization program. A sum of $420,000 was allotted to Kansas alone to provide for vaccine and administration of an immunization program. This money must be spent by February 1956. Is this a precedent being set by the federal government for all future immunization programs, or was such legislation passed to control the vaccine until the supply reaches the demand?

Federal aid to education, compulsory disability coverage under the Social Security Act, tax deferred retirement plans, treaty power, etc., combined with federal legislation before mentioned, will play an intricate part in the future of the medical profession when Congress reconvenes in 1956.

It behooves every state and county medical society —yes, every physician—to support the A.M.A. in its endeavor to pass legislation which benefits the public or to reject such bills which have no apparent advantage. It is equally important for the A.M.A. to send information about proposed legislation to state and county component groups so that the individual physician has an opportunity to know what is being considered in Washington.

Federal Aid Programs

Several years ago the JOURNAL carried a series of articles describing the various Kansas programs which were aided by federal appropriations. A new report on federal aid offers material for reflection, so without comment on any phase of this subject here are a few facts supplied by the American Medical Association Washington office.

The federal government is interested in many health programs administered by some 20 separate bureaus including the Children's Bureau, the United States Public Health Service, the Veterans Administration, the Department of Defense, and the Treasury Department. Some programs are operated from the national level and others by the states with federal money. Details of any program will be supplied upon request, but this story is a more general one.

In the fiscal year ending June 30, 1954, the federal government appropriated $1,775,882,197 for health projects. In 1955 this figure was $2,131,820,372. For this fiscal year ending June 30, 1956, health appropriations are $2,268,826,576. So in the last three years this item of federal expense has risen by almost $500 million!

Health, Education, and Welfare, the Defense De-

partment, and the Veterans Administration will each spend more than a half billion dollars on health this year. The total of two and one-quarter billion dollars is of some consequence even in a multi-billion dollar budget.

For instance, the health figure is 15 times the amount needed to maintain Congress and the federal courts. It is 14 times the budget of the State Department and is four times more than is spent either by the Labor Department or the Post Office Department.

The federal government now buys 15 per cent of all the health service in the nation. In other words, for every dollar public and private health expense, including tooth paste and cancer research, the federal government pays 15 cents.

This also reflects in the Kansas health picture. The health figure for federal grants to Kansas for 1955-1956 is not immediately available, but a somewhat more inclusive figure is. In 1945 Kansas received about $10 million federal aid for all purposes, health as well as welfare, education, highways, etc. In 1954 this was more than $40 million. Incidentally, the total Kansas budget in 1945 was $60 million, which rose in 1954 to $218. Last year another $6.5 million was added, and the end is not yet in sight.

On Public View

Doctors as a group receive the confidence and respect of the public, according to a report issued recently by the Los Angeles County Medical Association on completion of a public opinion survey conducted over a period of three months. The finding differs sharply from results of other recent opinion samplings in scattered areas of the nation which indicated widespread "public hostility" toward the medical profession.

There is no reason to suppose that Kansans would subscribe to the opinions expressed in California. Neither is there reason to believe that residents of this state are as dissatisfied with their doctors as are those who were queried in other localities. At any rate, a study of the Los Angeles survey may serve to enlighten the physician here on areas in which misunderstanding often exists.

In conducting the study the John B. Knight Company of Los Angeles interviewed 360 adults. An "influence" group of 51 persons was selected arbitrarily to represent as nearly as possible a cross section of those persons whose position put them into a category of leadership. There were 309 in the group representing the "general public."

Thirty-eight phases were covered in the survey report. Included here are only those items which seem to be of particular interest in Kansas.

Surprisingly, 75.1 per cent had a regular or family doctor.

Persons who felt that their physicians had given them all the information they wished about their illnesses made up 91 per cent of the group.

The doctor's attitude was approved by 85.5 per cent as "kindly, sympathetic." Approval of the amount of time spent on diagnosis and treatment was voiced by 95.2 per cent. Only 15 per cent reported having called a physician who couldn't take the case, and 61.3 per cent of those felt that the doctor was doing his best but was too busy. In selecting a doctor 64.2 per cent reported that they rely on the recommendations of a friend, and 2.5 per cent had called the county medical society for referral. More than half had changed physicians because of dissatisfaction. Reasons, in the order of their frequency, were: "Not thorough," "Didn't like his medication," "Not a specialist," "He charged too much."

How many believed that an osteopath is a medical doctor who has specialized? The answer is 77.5 per cent. And 83 per cent confused internists with interns. Confidence that a doctor would not undertake procedures for which he is not qualified was expressed by 86.5 per cent, another 6.3 per cent had doubts, and 7.1 per cent had no opinion. The public generally was of the opinion that "all" doctors were more competent to diagnose different diseases than to perform different surgical procedures.

Most were lenient about waiting for the doctor to keep appointments, 82.8 per cent feeling delay is justified and 10.5 per cent finding delays "unreasonable." Emergencies were cited as the reason for the doctor's delay by 44.5 per cent of those queried, but 20.9 per cent felt that appointments were scheduled too closely together.

The following figures reflect opinions on economics: 88.0 per cent were entirely satisfied with physicians' fees; 30.2 per cent felt that medical fees "generally" are unreasonable; 22.1 per cent thought they knew of people who needed medical treatment who weren't receiving it because doctors' fees are too high. Among community leaders 48 per cent had the latter opinion. The most frequently suggested causes for physicians' expenses were equipment, tools, utilities, and rent, in spite of the fact that 74.8 per cent thought the doctor's professional education required eight or more years.

The public guess on physician income, reduced to a median, was $17,581. A little more than 63 per cent thought that the doctor's income, whatever it is, is "about right," 7.3 per cent thought it too low, and 12.2 per cent had no opinion. More than 80 per cent would expect to find two cars in a doctor's garage.

Questions about insurance revealed that 74.3 per cent were more interested in having coverage for

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hospital bills than for doctors' fees; 59.8 per cent preferred "service type" insurance; 28.8 per cent wanted "indemnity," and 7.4 per cent like "closed panel" coverage. Compulsory health insurance would not be favored by 82.1 per cent, that figure rising to 91.5 in the "influence" group.

Questions that reflect opinion on matters of ethics disclosed that 66 per cent consider fee splitting wrong and 20.5 per cent approve. The belief that doctors send patients to particular pharmacies was held by 50.2 per cent, and 33.9 per cent think the physician receives a "rebate" from the pharmacy.

The medical society in Los Angeles listed 13 objectives when it undertook the survey. It appears that the information obtained will be valuable to that group in planning future public relations programs and is of interest to all who practice the art as well as the science of medicine.

Resigns from Editorial Board

Dr. Glen R. Shepherd, Kansas City, who has been an associate editor of the JOURNAL since 1949, resigned that position last month when he announced that he had accepted an appointment as assistant secretary of the Council on Medical Education and Hospitals of the American Medical Association.

In addition to serving as assistant to the dean at the University of Kansas School of Medicine during recent years, Dr. Shepherd has been assistant professor of medicine at the school, has written a nationally syndicated newspaper column, "Doctor's Notebook," and has contributed countless hours to the work he did for the JOURNAL. That has included assembling scientific material for the annual University of Kansas School of Medicine issue, editing clinicopathological conferences, and serving as liaison between the school and the publication.

The newly created position Dr. Shepherd has accepted with the A.M.A. has the specific assignment of spearheading further studies in the area of postgraduate medical education, reviewing and analyzing what is currently being done in all parts of the country in postgraduate medical education, and eventually recommending to the council ways in which it can be most helpful to physicians. Members of the Kansas Medical Society, and particularly those on the Editorial Board who have worked with Doctor Shepherd, wish him well in his new undertaking.

Dr. Vernon E. Wilson, assistant dean in charge of student affairs at the medical school, has accepted the responsibility of serving as associate editor of the JOURNAL. He is now working with the Editorial Board on plans for future issues. Dr. Jesse D. Rising will edit clinicopathological conferences published after December, 1955.

ACTIVITIES OF MEMBERS

Dr. William C. Menninger, Topeka, was recipient of the 1955 honor award given by the Mississippi Valley Medical Society at its meeting in St. Louis last month. The award is reserved for non-members of the society "who have made distinguished contributions to clinical medicine."

Dr. Dale Peters, Wichita, was speaker at a recent meeting of the South Central Association of Social Workers. The meeting was held in Wichita.

Dr. Spencer Bayles, who has been assistant professor of medicine and of psychiatry at the University of Kansas Medical Center, is leaving this month to join the psychiatry faculty of Baylor University School of Medicine, Houston.

Dr. John C. Mitchell, Salina, has accepted appointment as a member of the Board of Education there to fill an unexpired term.

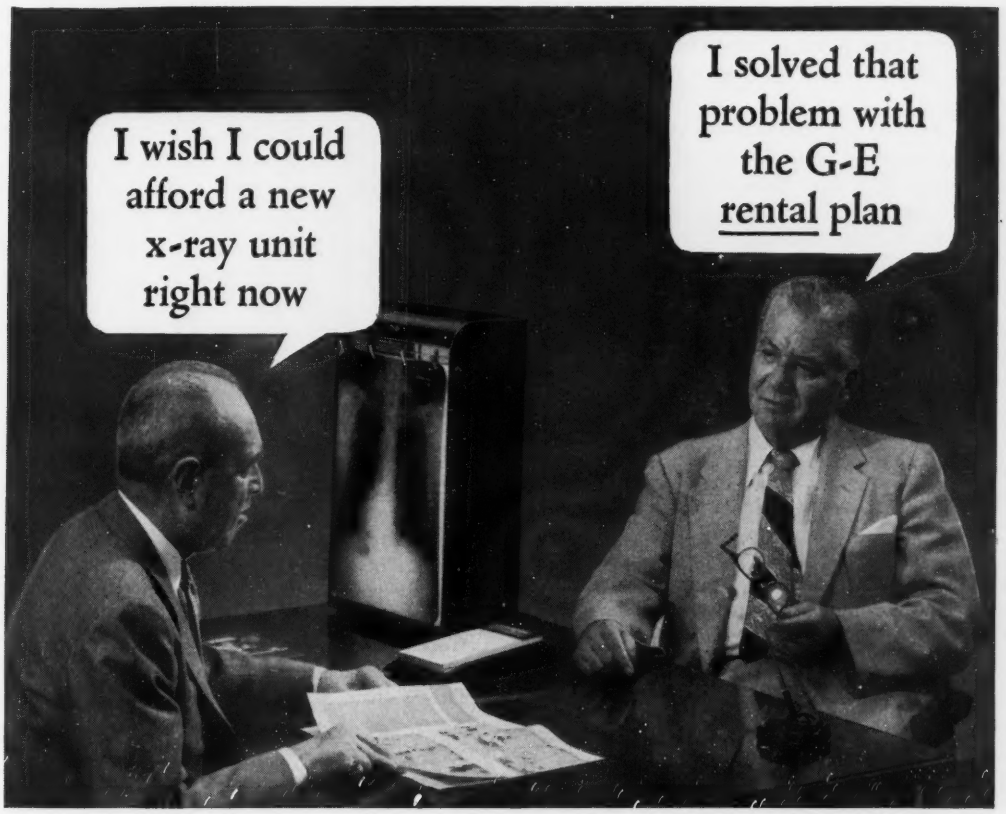
Dr. Karl E. Voldeng, Wellington, was guest speaker at a meeting of the Belle Plaine Parent-Teacher Association on October 10. He discussed the health of the school child.

A feature story about Dr. John L. Lattimore, Topeka, and the Lattimore-Fink Laboratories was published in the October 9 issue of the *Topeka Daily Capital*.

Dr. Eldred V. Thiehoff, of the University of Kansas Medical Center, has been made a fellow of the newly established American College of Preventive Medicine. He is also chairman of the committee on local arrangements for a November meeting of the Association of Teachers of Preventive Medicine.

Dr. C. R. Rombold, Wichita, addressed members of the Southwestern Bar Association at a meeting held at Hutchinson recently. He discussed disability evaluation.

Dr. Charles C. Gilkey has announced that he will devote full time to practice in Perry after January 1. At present he is under contract at the Santa Fe Hospital, Topeka, for half-day service.



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Dr. Harry Last, Leon, was the subject of a feature story in the *Leon News* on September 22.

Dr. J. Cotter Hirschberg, of the Menninger Foundation, Topeka, and Dr. Mary T. D. Glassen, Phillipsburg, took part in a joint meeting held in Salina recently by the Kansas Family Life Association, the Kansas Association for Mental Health, and the Kansas Council for Children and Youth.

Dr. Richard L. Merkel, Topeka, and Dr. M. D. McComas, Concordia, became fellows of the International College of Surgeons at a meeting held recently in Philadelphia.

Dr. Hansel D. Benvenuti, formerly of Wichita, has announced opening of an office in Huntington Park, California.

Dr. William L. Valk, of the University of Kansas Medical Center, participated in a panel on geriatrics at a recent meeting of the Mississippi Valley Medical Society in St. Louis.

Dr. David R. Davis, Emporia, discussed Salk vaccine at a recent meeting of the Outlook Club in Emporia.

An issue of the *Kansas City Star* last month carried a story about Dr. Paul W. Schafer and a recent study he made of medical facilities in Russia. Dr. Schafer, formerly at the University of Kansas Medical Center, is now a major in the medical corps of the Army.

Dr. John B. Dixon, Parsons, recently became a diplomate of the American Board of Ophthalmology.

Dr. Clarence W. Erickson, Pittsburg, immediate past president of the Kansas Heart Association, was recently appointed to the Board of Directors of the American Heart Association for a three-year term.

Dr. Lloyd W. Hatton, Salina, was guest speaker at a recent meeting of the Saline County Medical Assistants' Society. His address was on the subject of mental hygiene.

Dr. Harold M. Glover, who has been associated with the Axtell Clinic in Newton since 1916, recently announced his retirement from active practice. Members of the staff and employees of the clinic and of Axtell Christian Hospital and their families were present at a picnic in Dr. Glover's honor on October 11.

Dr. Cyril V. Black, Pratt, discussed the use of narcotics at a recent meeting of the Woman's Auxiliary to the Pratt County Medical Society.

Dr. G. Loren Norris, Winfield, president, and Dr. D. R. Bedford, Topeka, president-elect of the Kansas Heart Association, were delegates to the annual assembly of the American Heart Association held in New Orleans, October 21-26.

COUNTY SOCIETIES

Dr. Harry Statland, associate in medicine at the University of Kansas Medical Center and author of a recently published book on fluids, addressed the Shawnee County Medical Society at a meeting held in Topeka on October 3. His subject was "Syndromes of Fluid Imbalance—Recognition and Treatment."

Dr. William L. Warriner, 93-year-old physician who was the subject of a feature story in a recent issue of *Coronet,* was given a standing ovation.

A meeting of the Central Kansas Medical Society was held at the country club in Ellsworth on September 15. Members of the Auxiliary were guests of the Society at dinner.

Members of the Cloud County Society were hosts to the Golden Belt Medical Society at a meeting held at the country club in Concordia on October 13. Dr. Frank F. Allbritten, Jr., of the University of

DEATH NOTICES

CHASE B. JOHNSON, M.D.

Dr. C. B. Johnson, 64, a Lawrence physician who was an active member of the Douglas County Medical Society, died at Lawrence Memorial Hospital on October 7 after a short illness. A graduate of Northwestern University Medical School in 1921, Dr. Johnson came to Kansas in 1922 and opened an office in Eudora. He remained there until 1946 when he began practice in Lawrence.

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Kansas Medical Center, spoke on "The Surgical Treatment of Acquired Heart Disease." A panel discussion on diabetes was presented by Dr. Neil Jenkins, Salina; Dr. Robert H. O'Neil, Topeka; Dr. Edward J. Ryan, Emporia, and Dr. Henry Stryker, Jr., Concordia.

A meeting of the Northwest Kansas Medical Society was held at Colby on September 28. The subject for discussion was distribution and administration of Salk vaccine.

Dr. George J. Thomas, chairman of the Section on Anesthesiology at the University of Pittsburgh, was speaker at a meeting of the Sedgwick County Medical Society held in Wichita on October 4. His subject was "Safeguards Against Explosions of Anesthetic Agents."

A meeting of the Tri-County Medical Society was held in Harper on September 21. Dr. Katherine Pennington, Wichita, spoke on "Pediatric Cardiology."

A meeting of the Wyandotte County Society was held at the Town House Hotel, Kansas City, on October 18. A movie, "Kidney Function in Health," was followed by discussion.

Dr. M. M. Tinterow, Wichita, was speaker at the September meeting of the Butler County Society in El Dorado. His subject was "What's New in Anesthesiology."

Foundation Assists in Office Financing

The Sears-Roebuck Foundation, in cooperation with the American Medical Association, has announced a new plan for assistance in establishing medical practice units with loans of up to $25,000. The unsecured, low cost, 10-year loans will be available to physicians seeking to establish new practices but unable to arrange full local financing. A grant of $125,000 is available to begin the program.

The plan requires that the physician first exhaust all local possibilities for financing, that his application indicate a need for a practice in the proposed locality and good possibilities for success and public service, and that he give evidence of effort and thought in planning a well organized, effective practice unit. As grants are repaid, the money turned back into the fund will be used for establishing further units.

The plan relies on individual initiative and enterprise, requires that assistance be given only where it will generate independence, and is sustained entirely by those who benefit from it. Continuation of the plan after this year depends on its reception and support by the medical profession.

Boston Clinical Session

This year's American Medical Association clinical meeting in Boston, November 29 through December 2, is expected to be the largest ever held. The program, aimed at helping to solve the daily practice problems of the family physician, will probably attract some 4,000 physicians. About 200 scientific papers and exhibits have been scheduled for presentation.

Closed circuit television programs, originating in New England Deaconess Hospital, will bring live operations in color to the lecture hall. The program is being sponsored by Smith, Kline and French Laboratories.

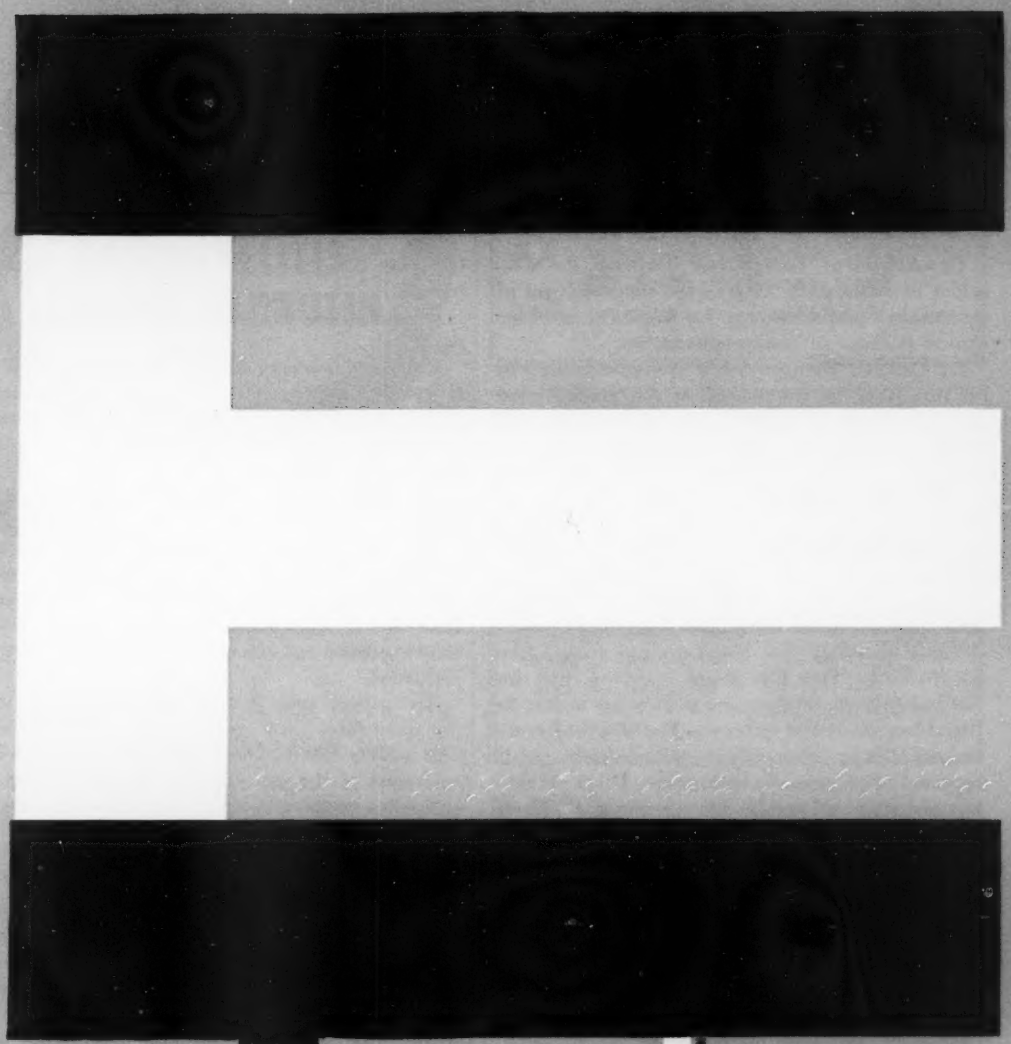
More than 50 motion pictures will be shown during the session, and 150 technical exhibits will be displayed. Registrants at the meeting will receive tickets to a concert given by the Boston Symphony as a courtesy of Winthrop-Stearns, Inc.

Grants Total $100,723

Recent grants to the University of Kansas Medical Center make a total of $100,723 available for research at the institution. The American Cancer Society has awarded $32,100 for work under the supervision of Dr. Robert E. Stowell on "Physical, Chemical, Structural, and Functional Changes Associated with Cancer," and the Kansas Division of the American Cancer Society has added $15,000. The National Cancer Institute has authorized a grant of $18,101 for a project entitled "Histochemical Studies of Necrosis."

Two amounts were received from the U.S. Public Health Service. The first, $25,000, is for a study on "Evaluation of Sera Diagnostic Tests for Cancer," to be supervised by Dr. Jack Hill and Dr. Stowell. The second, $10,522, will be devoted to "Studies of Liver Function in Experimental Cirrhosis" conducted by Dr. Chauncey G. Bly.

The Kentucky State Medical Association's Veterans Committee advocates the presence of a physician at American Legion post meetings to create a better understanding of medical problems as they affect the veteran and the public. Since Legion policies regarding such problems originate at the local level, the profession as a whole would benefit if the Kentucky plan became universal.



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Panhypopituitarism: Problems of Etiologic Diagnosis and Therapy

Tumor Conference

Edited by Bernard Klionsky, M.D.

Dr. Allbritten: Today's case illustrates the difficulties of establishing an etiologic diagnosis and of determining proper therapy for a patient who has clinical evidence of panhypopituitarism.

Dr. Calkins: The patient is a 39-year-old man who for two years has complained of the gradual onset and progression of weakness, anorexia, nausea and vomiting, weight loss, loss of libido and of potency, intolerance to cold, and loss of body hair. Three months ago he sought medical attention; therapy with hydrocortisone and thyroid was instituted. One month ago he became too weak to continue work and sought hospitalization.

Physical examination revealed a chronically ill man who appeared in no acute distress and who showed evidence of weight loss. Blood pressure ranged from 80-120/60-80. Hair was absent from the chest and was scanty in the axillary and pubic areas and at the lateral border of the eyebrows. The skin was coarse and dry. His face was puffy, he talked slowly, and he appeared to be generally underactive. His testes were soft and atrophied and his prostate was small. Visual fields were normal.

Steroid and thyroid therapy were discontinued at the time of hospitalization. Initially the serum electrolyte pattern was normal. Within five days the serum sodium and chloride fell to 111 mEq/1 and 87 mEq/1 respectively; the patient felt markedly weaker and developed increased nausea and vomiting. Oral administration of sodium chloride was followed by clinical and subjective improvement.

His basal metabolic rate was −20. Protein bound iodine was normal at 4.7 gamma per cent, I^{131} uptake studies revealed 2 per cent uptake in 24 hours. Following the administration of 10 cc. of thyroid stimulating hormone (TSH) intramuscularly, the I^{181} uptake was increased to a normal level. This emphasizes the fact that his thyroid is capable of responding to pituitary stimulation. Administration of 25 mgms. of ACTH was followed by a drop in the circulating eosinophile count from 211 to 78/cu. mm. Seventeen ketosteroid excretion in 24 hours was 6 mg., which is below the limits of normal. The 11-oxysteroid excretion was 0.7 mg., which is within the range of normal.

Dr. Allbritten: Are there pertinent radiologic findings?

Radiology resident: All our findings are negative. It was felt that the sella tursica was within normal limits of size. There were no erosions. Intravenous pyelograms and roentgenograms of the chest and sinuses were normal.

Dr. Allbritten: Dr. Delp, would you discuss this case?

Dr. Delp: For several years this patient has presented a problem to his physician, who felt correctly that he had an atypical adrenal cortical insufficiency. His tentative diagnosis was Addison's disease, but he wasn't satisfied and referred the patient for complete evaluation.

The patient states that his initial complaint, starting about three years ago, was that of loss of libido. One notices the thickness, puffiness, and lardaceous coloration of the patient's skin. One can't help but notice the complete absence of hair on his face. He tells you that he shaves now only once a week. His hair, rather than being coarse, is extremely fine, and I am certain that in the past four or five years it has changed in texture. One also notices that he is losing his eyebrows and that his skin lacks pigmentation.

Here is a patient who has myxedema, immediately evident by inspection. There are symptoms and signs of adrenal cortical and of testicular insufficiency. These things we can verify. One immediately looks for something that can account for all these coexisting phenomena; one must think of pituitary deficiency, probably caused by tumor.

Pressure on the optic chiasm by an expanding pituitary tumor may produce bitemporal hemianopsia and eventual blindness. Several years ago I observed this complication in a patient whose initial symptoms and findings were almost identical with this man's. Can loss of vision be prevented?

Dr. Allbritten: Dr. Williamson, would you discuss the neurosurgical aspects of this case?

Dr. Williamson: One look at the man leads one to think that he has a pituitary tumor. In attempting to prove it one falls short in two spheres. One is the x-ray evidence of the normal size of the sella tursica, and the other is the absence of neurologic involve-

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ment of the optic chiasm which is just above the sella. Ordinarily a chromophobe pituitary adenoma begins to grow within the sella tursica. Before it breaks out enough to compress the optic chiasm and cause loss of vision, it usually causes enlargement of the sella evident on roentgenograms. Normal sized sellas are reported in cases of pituitary adenoma which originate from the pituitary stalk. However, a tumor arising above the sella tursica would be even more likely to involve the optic nerve or optic chiasm. This man has absolutely normal visual fields and normal appearing optic discs with no trace of optic atrophy.

The question for the neurosurgeon is whether there is enough evidence of pituitary adenoma to justify (1) surgery, (2) x-ray therapy, or (3) further studies in an attempt to prove the diagnosis. A carotid arteriogram is a helpful diagnostic study. The carotid artery runs along the sella tursica and just above it and is displaced by a pituitary tumor. A pneumoencephalogram could be considered, but it is not very satisfactory in outlining a lesion in that region. We considered both these studies and still could do them. However, such procedures may be stressful and shocking, particularly for a patient with hypoadrenalism.

Regardless of what such procedures might show, if he does have a tumor above the sella tursica, from the practical point of view it is going to stay there. The neurosurgeon does not operate on pituitary adenomas in order to change the endocrine status, because he cannot improve it. He operates solely to save vision, and this man has lost no vision. If this patient has a glioma of the hypothalamus, it, too, is inoperable. It is difficult to decide what to do for this man. I am afraid, as is Dr. Delp, that eventually the pathologist will make the diagnosis of glioma of the hypothalamus or of a very atypical chromophobe adenoma. This is a most interesting and difficult problem, and the practical thing I can answer—that is, we can't cure him with an operation.

Dr. Allbritten: How does this differ from Simmonds' disease, Dr. Delp?

Dr. Delp: True Simmonds' disease is similar to this. Simmonds' disease is an endocrine disorder with profound panhypopituitarism. There has been much confusion between it and anorexia nervosa, simply because of the cachectic state into which both diseases led. This man has no diabetes insipidus. His adrenal cortical insufficiency has been fairly well controlled with cortisone up to the present, and can be controlled in the future. There is no reason why he should become cachectic if he does develop diabetes insipidus.

Dr. Stowell: The neurosurgeon thinks that this patient is not a candidate for surgery. Does the radiologist think he is a candidate for irradiation?

Dr. Germann: We must admit that this man is hypopituitary. Irradiation would only aggravate the situation. There is no convincing evidence, at least as yet, that this is a proliferating tumor. The radiotherapist uses irradiation for the same reasons that the neurosurgeon operates: to save vision or stop the progression of growing tumor. Under present circumstances we would not be justified in the use of radiation therapy.

Dr. Allbritten: Would radiation therapy to a pituitary neoplasm alleviate his hypopituitarism?

Dr. Germann: No.

Dr. Allbritten: Dr. Brackett, do you have any comments?

Dr. Brackett: I think that there is considerable doubt about the diagnosis of a pituitary adenoma. Patients with chromophobe adenomas usually have enlarged sellas and complain of headache by the time that loss of libido and signs of adrenal insufficiency are present.

This man's atypical history suggests the absence of a tumor. A tuberculous granuloma must be considered as a diagnostic possibility.

Dr. Allbritten: Since neither surgery nor irradiation is indicated at present, what should be the plan of management?

Dr. Delp: Therapy with thyroid, cortisone, testosterone, and ACTH will be instituted to control the endocrine imbalance.

Although a definite etiologic diagnosis has not been made, the probability is that the pituitary lesion is a chromophobe adenoma. Signs of visual impairment may develop, and neurosurgery may eventually be necessary to prevent blindness. Periodic examinations at approximately three-months intervals should include roentgenograms of the skull and evaluation of the visual fields.

Editor's note: After ten months the patient's endocrine disorder has been controlled by replacement therapy as indicated, and he has returned to work. No visual disturbances have developed, but continued observation is indicated.

The 1956 meeting of the Kansas Medical Society will be held in Topeka, April 29-May 3.

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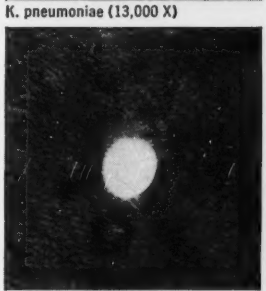

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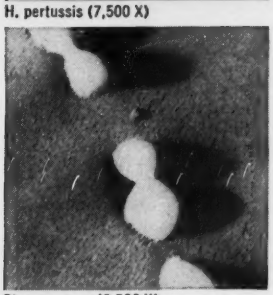

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THE MONTH IN WASHINGTON

Editor's Note. The following summary of Washington news was prepared by the Washington office of the A.M.A. for distribution to state and regional medical journals.

Within a few months there will be under way the first comprehensive survey ever to be made of the nation's mental health problems. The study will attempt to measure the extent of mental illness, to judge the progress and lack of progress in research, and to estimate the additional hospitals and clinics and trained personnel needed before a start can be made toward a solution.

A newly-formed Joint Commission on Mental Illness and Health already has begun preliminary work on the survey. The all-out effort will be initiated—possibly before the first of the year—after the Commission has received the formal approval of the National Mental Health Advisory Council of U.S. Public Health Service and the Surgeon General. Once this endorsement has been given, $250,000 in U.S. funds will be available to help with the first year's operations. Another million dollars is to be supplied over the following two years.

Originally, the Joint Commission was formed by the American Medical Association's Council on Mental Health and the American Psychiatric Association. Later other associations joined in, including the American Association of Psychiatric Social Workers, the American Hospital Association, the American Nurses Association, the National League of Nursing, the American Psychological Association, and the National Education Association.

A nationwide survey has been the objective of these associations for more than a year. Substance was added to the idea this year when Congress approved the $1,250,000 fund, to be used over three years, for a comprehensive study. The law specifies that the investigation be conducted by non-governmental bodies; to fully qualify, the Joint Commission has been legally incorporated.

At hearings before Congressional committees early this year psychiatrists and others outlined the complex problem they are facing.

The care of mental patients is one of the great financial burdens of the states; rate of cure and rehabilitation is so low that institutions are being filled as fast as they can be constructed; half the hospital beds are occupied by mental patients, and their care costs more than a billion dollars a year in tax funds.

There are not enough psychiatrists trained to administer state programs or even all the large hospitals; competition for the top men in this field has been compared to the proselyting of football players and coaches.

Many of the leading psychiatrists complain that too much attention is being paid to constructing hospitals and not enough to research, which might develop treatments that would keep many patients out of institutions and bring about the rehabilitation of hundreds of thousands of others now hospitalized.

In testifying before a House committee early this year, Dr. Leo H. Bartemeier, representing the A.M.A., argued for federal help in conducting the survey. He told the committee: "For several years we in the profession of psychiatry have been aware of the critical need for a survey and evaluation of our facilities and programs for the diagnosis, treatment, and care of the mentally ill and retarded. While the problems of mental illness appear to grow in almost geometric proportion, we find ourselves without a comprehensive, up-to-date, integrated body of knowledge in spite of the fact that many worthwhile surveys and studies in this field have been made. It is only with such complete knowledge that our present and future direction and programs can be properly planned."

NOTES

Before it prepares a report on the narcotic problem, the Senate subcommittee will have held hearings in most parts of the country. Many local addiction problems have been described. At the New York hearing, the subcommittee was urged to recommend a system of clinics, where the addict legally could obtain narcotics at reasonable cost, thereby defeating the rackets.

Although states either may take U.S. grants to buy Salk vaccine or the vaccine itself, most of them are taking the money.

Veterans Administration has set up a seventh area medical office in Columbus, Ohio, a move that it believes eventually will provide better service at less cost.

Almost nine million dollars will be spent next year on health work in North, South, and Central America by international bodies, such as World Health Organization. One project is the starting in Mexico of a four-year malaria eradication program.

The Navy has set up a program for training Waves as nurses; they will be obligated for a year's active duty for each year of training.

Bureau of Internal Revenue has summarized deductible and non-deductible medical expenses for income tax purposes; the listings combine new interpretations with a clarification of old rulings.

The A.M.A. clinical meeting will be held in Boston, November 29-December 2.

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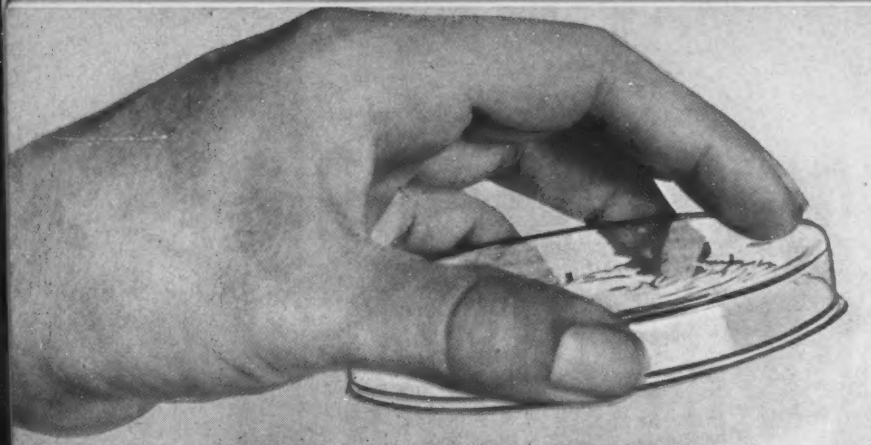

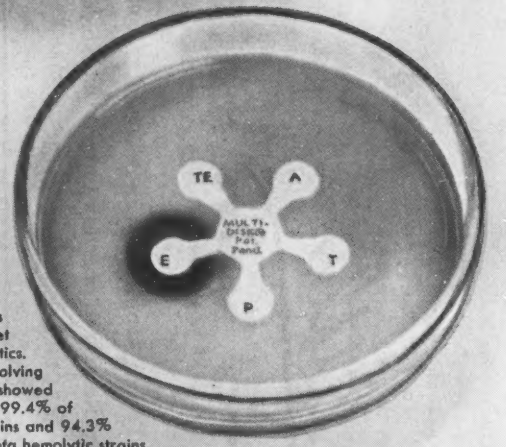

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1. Eisenberg, et al., Antib. & Chemo., 3:1026-1028, Oct., 1953.

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Hemodynamic Aspects of Hypertension with Special Reference to the Viscosity of Blood

William F. Casteen, M.D.

Kansas City, Kansas

This paper will attempt to examine the physiological relationships of blood flow and thereby seek to gain understanding of the pathological physiological mechanics of hypertension.

Hypertension is known to the physician by an increase in arterial blood pressure. Arterial blood pressure is but one aspect of the dynamic state of the circulatory system. Needless to say, understanding of a disturbance of this dynamic system can be based only upon knowledge of the physiological dynamics governing the system.

The term "hypertension" as used in this paper will be restricted to (1) those disease states where increase in blood pressure occurs secondary to chronic kidney disease; (2) the condition commonly known as "essential hypertension." The anatomical lesions occurring as a result of prolonged high blood pressure will not be considered.

I. THE CARDIOVASCULAR SYSTEM AS A SIMPLE CLOSED FLUID-FLOW SYSTEM

The cardiovascular system consists essentially of a group of highly branching fluid-conducting tubes establishing a fluid circuit about a pump, the heart. Friction exists in the flowing fluid and exerts a force tending to oppose the motion of the fluid. The heart exerts a force on the fluid system which creates blood pressure (force per unit area) and overcomes the frictional force.

The arterioles act as a valve tending to shut off or open up flow in the fluid circuit and are in turn controlled by neurogenic and humoral mechanisms. The pump is one of variable displacement and is also under the control of neurogenic and humoral mechanisms as to both stroke volume and frequency of contraction. The system is further complicated by the fact that the fluid conducting tubes are elastic.[1, 2]

Since the system is constructed around a mass in motion, the laws of basic mechanics must apply, and two entities are cardinal: force and mass. Since we are dealing with a fluid system, in general terms, pressure and volume may be considered. For a given fluid conduit:

$$\text{Rate of flow} = f(\text{pressure}) \times f\left\{\frac{1}{\text{resistance to flow}}\right\} \quad (1)$$

It should be noted that in this relationship, considering the conducting system, pressure and resistance are independent variables, and volume rate of flow is a dependent variable. Volume rate of flow and pressure can be measured.

In hypertension it has been demonstrated that the cardiac output is normal and the mean arterial pressure increased. Therefore, resistance must be increased also.

Considering the pump, volume rate of flow and resistance are independent variables, and pressure is a dependent variable. Hypertension may then be produced as a compensatory mechanism by the pump to maintain normal rate of flow in the face of increased resistance, or as a result of increased peripheral resistance protecting the capillary beds from a derangement in the pump tending to greatly increased cardiac output.

It will be assumed that the first alternative is the correct one. Hypertension then must be the result of a normal cardiac output in the face of increased peripheral resistance. Factors determining peripheral resistance will now be considered.

II. THE APPLICABILITY OF POISEUILLE'S LAW

In 1839 and 1840, Nagen and Poiseuille, working independently, enunciated the concept of laminar flow and the basic mathematical relationships of such flow.[3, 4] These relationships state that when laminar fluid flow occurs in a cylindrical tube, the rate of flow varies directly with the pressure drop and with the fourth power of the diameter of the tube, and inversely with the length of the pipe and viscosity of the fluid flowing:

$$V = \frac{\pi\, d^4\, w\, \Delta P}{128\, \mu\, L} \quad (2)$$

where:

- V = volume rate of flow
- d = diameter of the tube
- w = specific weight of the fluid
- ΔP = pressure drop between two reference points
- L = length of tube between reference points
- μ = absolute viscosity of the fluid

If the discharge pressure of the tube be held constant, it is seen that the pressure drop ΔP is proportional to

This is one of 11 theses, written by fourth year students at the University of Kansas School of Medicine, selected for publication by the Editorial Board from a group judged to be the best by the faculty at the school. This paper received first prize in the 1955 Phi Chi award contest. Dr. Casteen is now serving his internship at the University of Kansas Medical Center.

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1. Rosenberg, S. and Oster, K. A., "Gelatine in the Treatment of Brittle Nails," *Conn. State Med. J.* 19:171-179, March 1955.
2. Tyson, T. L., *J. Invest. Dermat.* 14:323, May 1950.

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the applied pressure P, and equation 2 may be written:

$$V = \frac{d^4 w\ P}{128\ \mu\ L} \quad (3)$$

Now L, d, w, and μ are factors associated with resistance to flow, and for any given system the resistance to flow R may be stated:

$$R = \frac{128\ \mu\ L}{d^4 w} \quad (4)$$

Substituting equation 4 in equation 3:

$$V = \frac{P}{R} \quad (5)$$

which is the form of Poiseuille's law commonly used by physiologists. It should be noted that equation 5 is a special form of equation 1, where fluid flow is of a laminar nature in a cylindrical conductor. Most investigators in circulatory physiology believe blood flow in virtually all parts of the peripheral circulation to be laminar in character.

Since blood pressure is elevated because of increased total peripheral resistance (R), if one accepts laminar flow, equation 4 must contain a factor or factors, a change in which results in increased peripheral resistance. Further, since the mean arterial pressure is known to be increased in the order of two or three fold during hypertension, a linear factor affecting total peripheral resistance need change only a corresponding amount.

The factors governing equation 4 for a given vessel segment are length of the segment, specific weight of the blood, the diameter of the segment, and the viscosity of the blood. Before examining each of these factors in detail it should be pointed out that since R varies inversely with diameter as a rather large exponential function (d^4), only the smallest vessels will contribute significantly to the effective peripheral resistance, hence one need only be concerned with relationships of flow in the arterioles and capillaries.

An increase in length of the individual arteriole by a factor in the order of magnitude of two or three fold would result in an increase in peripheral resistance comparable to that found in hypertension. Such anatomical change has not been reported by pathologists, but such a change in length of arterioles might be difficult to determine on study of microscopic sections.

A change in specific weight of blood by a factor in the order of magnitude of two or three fold is obviously impossible since the principal constituents of blood are present in normal concentrations in blood of hypertensives.

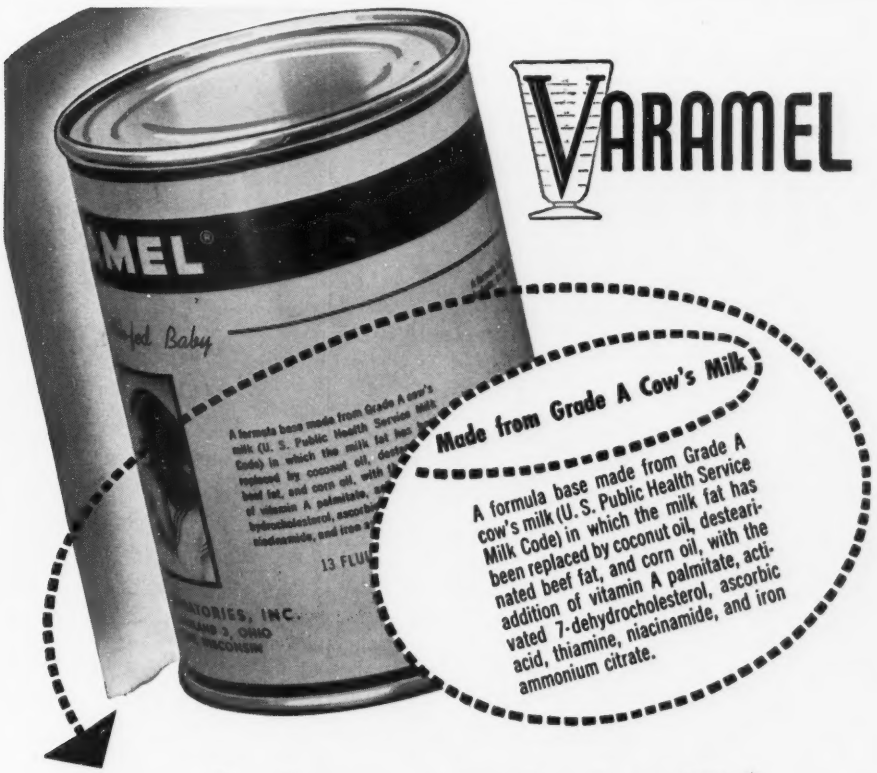
The ability of the arteriole to change diameter and its function in controlling circulation through the various hemic circuits of the circulatory system are well known. Most modern investigators assume that arteriolar constriction is the cause of increased peripheral resistance in hypertension.[5, 10]

As has been pointed out in the preceding discussion, the resistance to flow (assuming all other factors constant) and the mean arterial pressure vary inversely as the fourth power of the diameter of the arteriole. It is readily calculated then, that a reduction in caliber of an arteriole by 50 per cent affords an increase in resistance to flow of 16 fold. To increase resistance by 50 per cent the arteriolar diameter need decrease only by approximately 15 per cent. To increase resistance by 10 per cent, arteriolar diameter need decrease only 0.2 per cent. For a biological regulatory mechanism to operate at such tolerances would be most unusual. It seems most likely that all arterioles are not governed to this degree of accuracy, but that averaging obtains and peripheral resistance may be closely controlled by rather crude changes in diameter of large numbers of arterioles.

Since the vasomotor system, together with humoral agents, maintains and regulates blood pressure, it has long been assumed that hypertension is a result of a derangement of the regulatory mechanism. The humoral mechanism thought to be present inducing vasoconstriction in renal hypertension will not be considered.

Essential hypertension has been thought to represent a generalized neurogenic vasoconstriction caused by derangement in the neural regulatory mechanism. This theory has had its basis in "logical assumption" more than in experimental proof.[5, 11] Strong experimental evidence indicates that if vasoconstriction is an etiological factor in hypertension, it is not neurogenic in character.

Printzmetal and Wilson state at the beginning of their work on the nature of the peripheral resistance in hypertension,[7] "From the physiological point of view elevation of blood pressure may be due to an increase in cardiac output, in the volume or viscosity of the blood, or in the resistance of the peripheral vessels." They cite references establishing the normality of all but the last factor in hypertension. By direct application of heat, and by reactive hyperemia, vasodilatation was induced in the upper extremity of hypertensives and controls. The changes in blood flow were found to be equal in the two groups. The authors concluded that the increased peripheral resistance was due to generalized vascular hypertonus. By Novocaine injection of upper dorsal sympathetic ganglia, it was also shown that the generalized vascular hypertonus was not neurogenic in origin. These investigators suggested that *intrinsic* hypertonus exists in the arterioles. These experiments actually indicate that the vasomotor system in hypertension acts in a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normal manner and offers no evidence for or against reduced arteriolar diameter.

In more recent times, Kowalski et al.[12] measured changes in vasoconstrictor tone in the human lower extremity, in hypertensives and controls, using tetraethylammonium. Again, these investigators assume increased total peripheral resistance and arteriolar hypertonus to be synonymous. Their findings agreed with those of Printzmetal and Wilson, that the prevailing level of neurogenic vasomotor tone in the extremities was not found to be increased in patients with hypertension. Again, these experiments merely demonstrate increased peripheral resistance and that this increased resistance is not due to neurogenic vasomotor tone. No conclusions concerning the diameter of arterioles can be drawn.

Several German investigators in the early 1900's studied the viscosity of blood.[13, 22] Their studies were based on measuring the flow in a glass capillary tube arranged in a manner similar to that known as the Hess viscometer. The normal relative viscosity (viscosity relative to that of water) as determined by these investigators varied from 4.51 to 5.12, with percentage deviation of about four per cent. These investigators found rather marked physiological variations in blood viscosity.

Hess[16] and others showed that the viscosity of the blood varies with age, increasing as age advances. Adam[18] determined that viscosity does not vary directly with specific gravity. These investigators disagreed about the effect of erythrocyte concentration upon blood viscosity. Determann [22] noted, "though a fairly close parallel exists between the two, so many exceptions are found, that on the determination of the red-cell count, no safe inference as to the viscosity of the blood can be drawn."

Burton-Opitz,[19] on the other hand, stated that "the red corpuscles are the principal factor in determining the viscosity of the blood." Austrian[23] found that frequently erythrocyte concentration and viscosity varied in direct proportion, but in many instances no close parallelism could be proved. Austrian concluded that although erythrocyte concentration was important in determining viscosity, it was not the dominant factor. Austrian also found considerable variation in viscosity of plasma.

Determann[22] believed the viscosity of blood to be dependent at least to some extent on the osmotic tension between plasma and the erythrocytes. Burton-Opitz[20] found that the blood of dogs fed on meat has a higher viscosity than that of hungry dogs, or those on a low protein diet. He also found that food rich in fat increases the viscosity of the whole blood. Adam[18] studied viscosity of protein and salt solutions and found that all salts did not affect viscosity to the same degree. Koryani and Bence[21] found that the gaseous content of the blood affected its viscosity and determined that increasing CO_2 content increased viscosity.

Austrian demonstrated that by arranging for dogs to re-breathe, viscosity could be increased as much as 20 per cent. He studied viscosity of blood and plasma in several diseases. He found diminution of viscosity of blood in anemia proportional to the severity of the anemia, and an increased viscosity of plasma in polycythemia which did not vary as a linear function of the erythrocyte concentration. An increase in viscosity of plasma in polycythemia was also found. In cases of chronic nephritis with hypertension, no significant deviation of viscosity was found.

In 1913, Rothmann[24] measured the viscosity of blood by means of glass capillary tubes having a diameter between 0.1 mm. and 0.2 mm. He found that viscosity decreased progressively with increasing rates of flow until a critical rate of flow was approached (Figure 1). The rate of flow at which the viscosity became constant depended upon the diameter of the capillary tube. The effect was enhanced by increasing the relative concentration of erythrocytes.

Rothmann considered this phenomenon to be due to an interaction between the cells and the walls of the tubes, that is, in very small tubes the viscosity is not independent of the walls and the rate of flow. This phenomenon has also been interpreted as indicating that at higher velocity the cells are thrown into

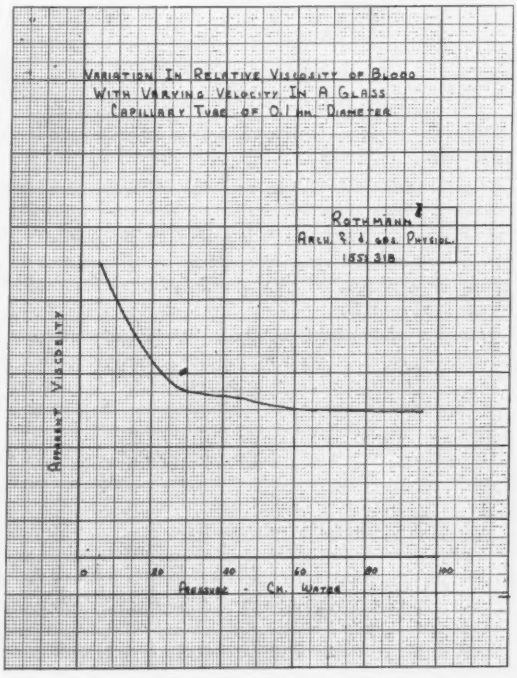

Figure 1

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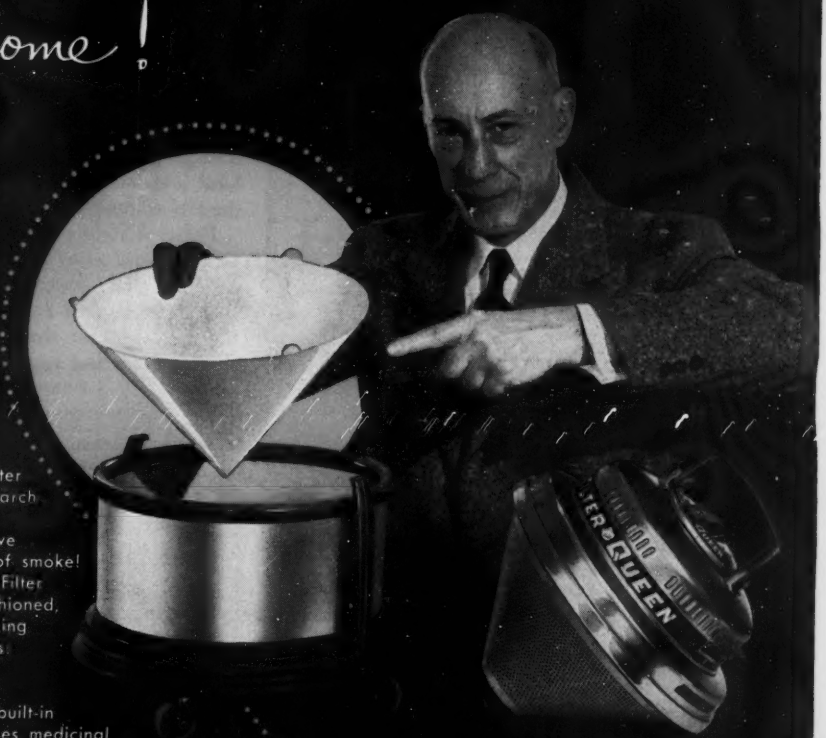

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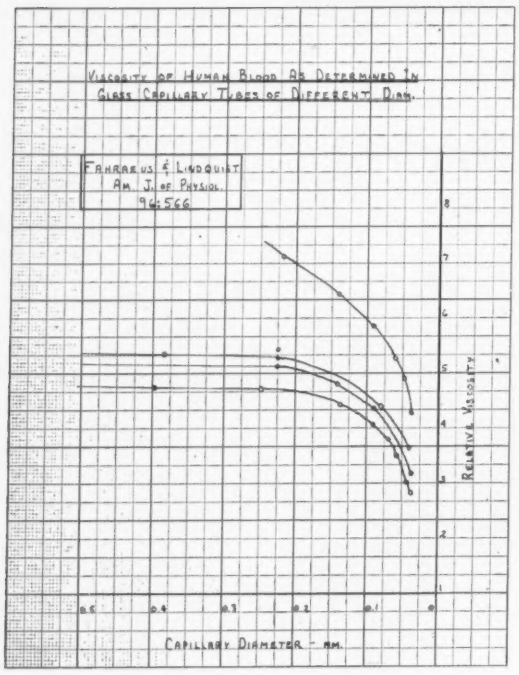

Viscosity of Human Blood As Determined In Glass Capillary Tubes of Different Diam.
Fahraeus & Lindquist
Am. J. of Physiol.
96:562
Relative Viscosity
Capillary Diameter - mm.

Figure 2

the center of the flow stream leaving only plasma in close contact with the walls and hence reducing the viscosity. It should be noted that the diameter of Rothmann's tubes was roughly ten times the diameter of a capillary. Hess had been aware of this phenomenon and had pointed out that in order to obtain accurate data with his viscometer, sufficiently high velocities must be used. Velocity was not standardized, however, and this may explain the different results obtained by early investigators using glass capillary viscometers.

In 1929, Harris and McLoughlin[25] studied the viscosity of blood in hypertensives with a Hess viscometer and reported that in 35 of 40 cases studied, viscosity was increased from 50 to 100 per cent. Systolic pressures only were obtained as an index of arterial pressure.

In 1935, Pickering,[6] using a glass viscometer, studied the viscosity of the blood in nine hypertensives. He found no correlation between systolic and diastolic pressure levels and blood viscosity.

It will be shown that measurements of viscosity of whole blood with a glass viscometer are misleading.

In 1931, Fahraeus and Lindquist[26] reviewed the work of previous investigators attempting to measure the viscosity of blood in narrow capillary tubes. They then measured the viscosity of blood in very accurately made glass capillary tubes of varying diameter. They used a pressure differential accurately standardized at 100 mm. Hg. Their results are summarized graphically in Figure 2.

This clearly indicates that viscosity is reduced with reduced diameter of the tube. "There seems to be no reason why the viscosity of the blood in still narrower tubes may not come very close to or perhaps coincide with the viscosity of the plasma. The law of Poiseuille does not apply to the flow of blood in capillary tubes of a diameter below about 0.3 mm." The arterioles and capillaries are vessels whose diameter is less than 0.3 mm. These investigators offer the theory that erythrocytes seek the center of the flow stream.

In 1933, Whittaker and Winton[27] reviewed the literature and pointed out, "The apparent viscosity of the blood flowing in the arterioles depends on the velocity of flow, the dimensions of the vessels, and possibly on other factors; it is evident that at the moment even the order of its value can hardly be predicted from the results of experiments on blood flow through glass tubes." These investigators perfused the hind limb of a dog at different pressures and noted the rate of flow (Figure 3 and Figure 4).

Figure 4 clearly shows the linear relationship indicating Poiseuille's law applies to blood flow in the extremity. The extremities used for perfusion were completely severed from the animal and determinations delayed for three hours to eliminate neurogenic reflexes and vasospasm.

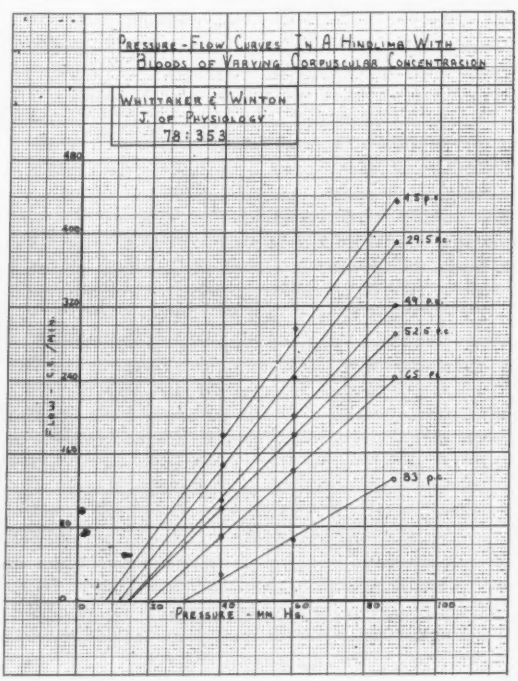
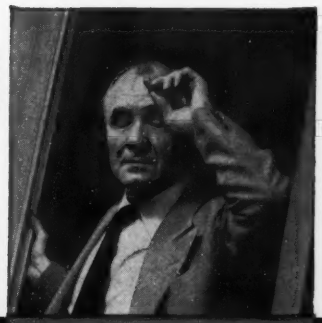
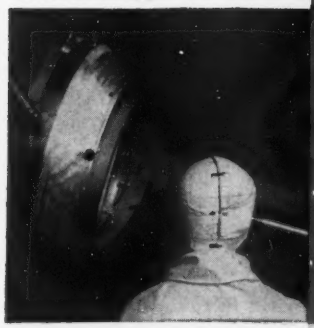

Pressure-Flow Curves In A Hindlimb With Bloods of Varying Corpuscular Concentration
Whittaker & Winton
J. of Physiology
78:353
Flow c.c./min.
Pressure - mm. Hg.

Figure 3

Ménière's syndrome, cerebral arteriosclerosis, fenestration surgery, streptomycin toxicity



radiation therapy



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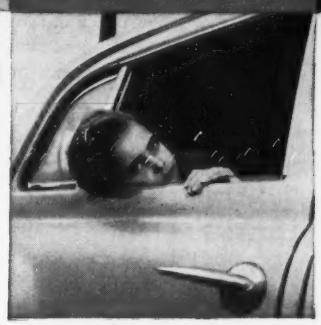

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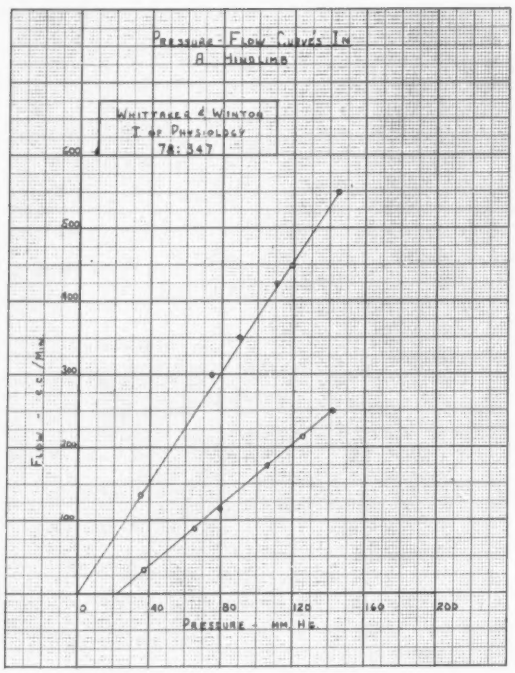

Figure 4

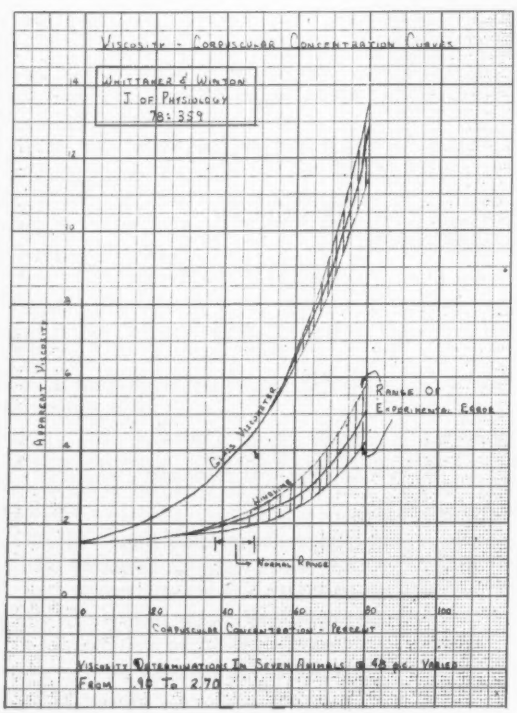
Viscosity - Corpuscular Concentration Curves
Whittaker & Winton
J of Physiology
78: 339
Apparent Viscosity
Range Of Experimental Error
Normal Range
Corpuscular Concentration - Percent
Viscosity Determinations In Seven Animals @ 48 sec. Varied From 1.9 To 2.70

Figure 5

The effect of erythrocyte concentration was demonstrated; the data are summarized in Figure 5.

The fact that a definite pressure was necessary to initiate flow, and that this pressure increased with increasing erythrocyte concentration, was interpreted as resulting from interaction between erythrocytes and vessel walls.

Whittaker and Winton also measured blood viscosity with a glass viscometer at varying erythrocyte concentrations. Figure 5 shows the relationship of viscosity so obtained with the viscosity obtained by perfusion, at different erythrocyte concentrations.

It is assumed that these investigators used blood of the animal from which the limb was obtained. Data are given for seven limbs. Viscosity varied as much as 50 per cent between different animals although erythrocyte concentration was essentially constant.

Evidence indicating that vasoconstriction does not alter the characteristics of flow was obtained. This is summarized in Figure 6.

From Figure 5 it is apparent that the viscosity of blood in the region where the greater part of peripheral resistance occurs is almost independent of the hematocrit and is for practical purposes identical with that of plasma. The work of early investigators on plasma viscosity, therefore, is essentially valid within the limits of their experimental errors.

Pappenheimer and Maes,[28] in 1942, performed experiments similar to those of Whittaker and Win-

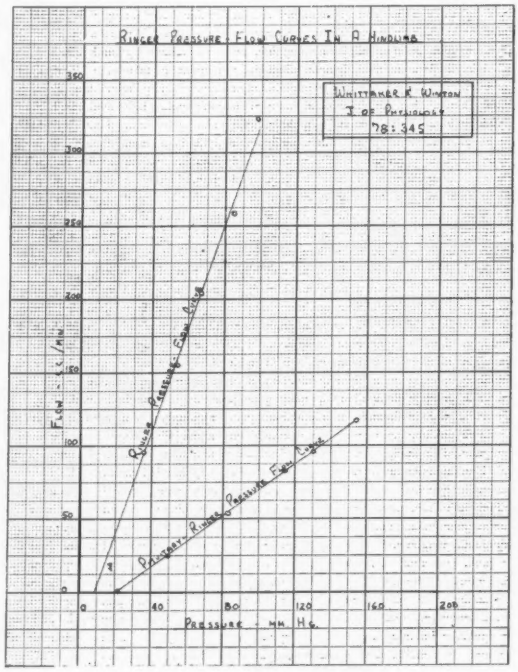

Figure 6

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ton, but used innervated limbs. Vasoconstriction was induced by various agents. Vasoconstriction was shown to increase apparent viscosity by as much as 70 per cent. They also showed that pressure-flow curves during vasoconstriction are linear only when the flow exceeds certain values, and that such curves

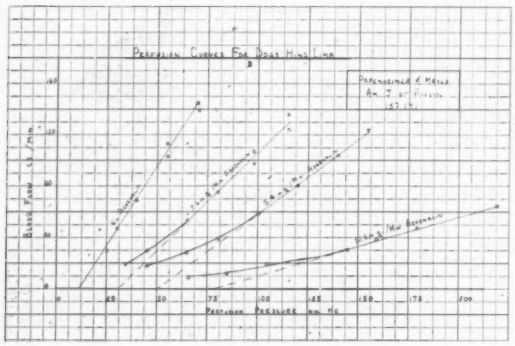

Figure 7

are parabolae about the flow axis and whose vertices lie at the origin (Figure 7). These investigators proposed the slope of the straight portion of the perfusion curve with Ringer's solution as an index of vasoconstriction. This probably represented the first logical suggestion for measuring even the relative diameter of an arteriole in vivo, indirect though it was.

In 1944, Green[29] et al. perfused dogs' hind limbs directly from the aorta and with innervation essentially intact. The pressure-flow curves obtained were parabolae about the flow axis whose vertices lay at the origin. The method of preparation of the limbs differed from the experiments of Whittaker and Winton and Pappenheimer and Maes, so as to more closely approach physiological conditions. The range of perfusion pressures was increased.

These investigators interpreted their results as indicating that the arteriolar diameter is increased mechanically by increasing arterial pressure and hence peripheral resistance is reduced by increasing arterial pressure when vasomotor tone remains constant. These investigators simply state, "Vasomotor activity remained practically constant at a high level," without indicating how this was determined. Without proof that vasomotor tone remained constant, one cannot be certain that the shape of the curve is not indicative of the form of response of vasomotor reflexes (vasodilatation as a reaction to increasing perfusion pressure). Since blood was supplied from the aorta, flow was pulsatile.

Thus attempts to measure viscosity of blood and relative arteriolar diameter have become intertwined. References citing plasma viscosity determinations in patients with hypertension on a rigorous basis with a large number of patients have not been found by this writer.

III. THE ARTERIAL PULSE PRESSURE

Although both the systolic and diastolic arterial pressures are increased in hypertension, the systolic pressure is increased out of proportion to the diastolic pressure, resulting in an increased pulse pressure.[30] Generally, the greater the elevation of systolic and diastolic pressures, the greater the pulse pressure.

The systolic and diastolic pressures represent only maximum and minimum values and do not give a complete picture of the variation of arterial pressure during the cardiac cycle. Tracings of arterial pressure have been obtainable for many years. Recently improved methods have been available, and the value

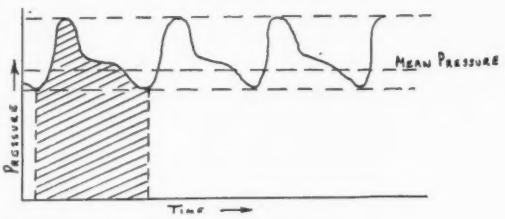

Figure 8

of such tracings in various pathological-physiological states of the circulation have been pointed out.

An arterial pressure recording from a large artery is sketched in Figure 8.

The mean pressure may be obtained by measuring the area under the curve for one cardiac cycle and dividing this quantity by the time required for the cardiac cycle. The mean pressure is the effective pressure in pushing blood out of arteries. The mean pressure cannot be calculated by averaging the systolic and diastolic pressures, and it must be appreciably lower than such an average. Considerable variation can occur in mean blood pressure with systolic and diastolic levels held constant. This can only be interpreted as reflecting changes in peripheral resistance, probably the degree of vasoconstriction of arterioles, despite the fact that systolic and diastolic pressure remained constant.

Peterson, Dripps, and Risman[31] have pointed out the advantages of actual mean pressure measurement and pressure wave interpretation. Volpitto, Woodbury, and Hamilton[32] have indicated the value of pressure wave interpretation in forecasting incipient shock in the surgical patient.

Upon inspection of Figure 8, it is apparent that the mean pressure more closely corresponds to the diastolic pressure than to the systolic pressure (normal individuals). Hence the diastolic pressure af-

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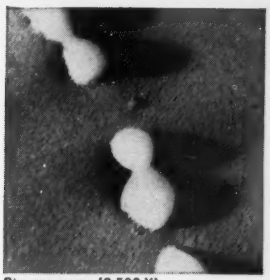
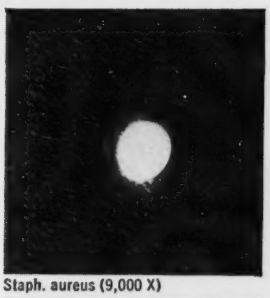


Str. pyogenes (8,500 X)



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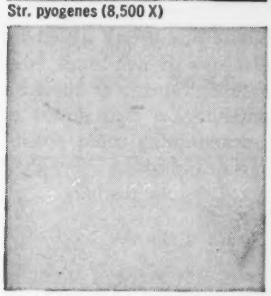
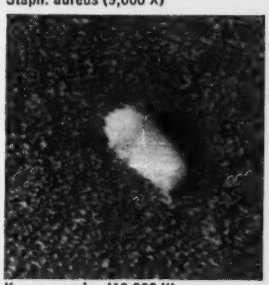
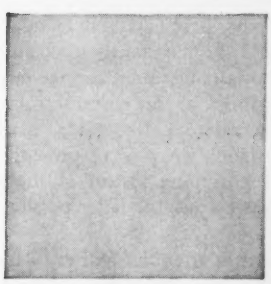
D. pneumoniae (10,000 X)





K. pneumoniae (13,000 X)

H. influenzae (16,000 X)



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fords a better index of total peripheral resistance than does the systolic pressure. This deduction agrees with the clinical observation that the peripheral vascular lesions of hypertensive cardiovascular disease correspond more closely with the diastolic pressure levels than with systolic pressure levels.

The heart, however, must do its work during systole, and hence the work of the heart will be closely correlated with the systolic pressure level. Cardiac hypertrophy and ventricular strain patterns should correlate more closely with systolic pressure levels.

The increased pulse pressure associated with extensive arteriosclerosis in elderly individuals is well known and is undoubtedly related to decreased distensibility of arterial walls.[33] Many hypertensives, however, show high pulse pressures without anatomical evidence of advanced degenerative changes in arterial walls.

Weiss et al.[30] studied cardiac output, blood volume, pulse wave velocity, and oscillometric measurements in hypertensives with different ranges of pulse pressures. These investigators concluded that augmented pulse pressures in hypertension were probably due to unknown changes in arterial and arteriolar walls.

Physiologists have been in disagreement as to whether peripheral resistance or arterial elasticity plays the dominant role in determining pulse pressure.

Wiggers[34] studied a circulation model and concluded that in elastic tubes with a linear volume-elasticity coefficient, increasing peripheral resistance reduced pulse pressure. This is in agreement with theoretical deduction. This may be interpreted as evidence that the volume-elasticity coefficient of the arterial system is not linear. Wiggers perfused the dog's aorta in situ and obtained a volume-elasticity curve. Difficulty in controlling leakage, however, made his data questionable.

Williams and Schroeder[35] obtained tracings of fall in blood pressure distal to occluded arteries in the dog. Arteries studied were those supplying single circulations such as the brachial, femoral, and renal. These investigators were attempting to evaluate peripheral resistance. They concluded that arterial elasticity played a relatively minor role in determining the shape of the curves they obtained, and therefore the volume-elasticity coefficient was essentially linear. Apparently this conclusion was based upon the fact that the rate of change of the slope of the early portion of their curves was essentially constant for varying blood pressures. Considering the relationship between rate of change of peripheral resistance and blood pressure demonstrated by Green et al., this conclusion is not justified.

Wiggers and Wegria[36] implanted a device on the aorta of living dogs to measure directly changes in distension of the aorta. When the measured distension was plotted against measured blood pressure, a straight line resulted up to a value of blood pressure ranging from 30 to 172 mm. Hg. for different animals, at which time a given increase in blood pressure produced a much smaller increase in distension than previous increments of blood pressure. This is shown graphically in Figure 9.

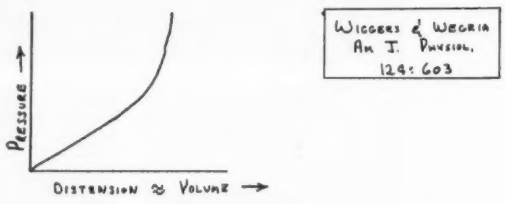

Figure 9

The dimensions and distensibility were found to vary with neural and humoral stimuli. If this work in the dog can be extended to human hypertension, it can be concluded that arterial distensibility plays the dominant role in determining pulse pressure, and the augmented pulse pressure of hypertension can be explained on the basis of non-linear arterial distensibility. The physiological role of altered arterial distensibility by physiological mechanisms is not clear. An increase in distensibility could possibly serve to reduce peak pressures encountered with rapid heart rate and augmented systolic discharge.

SUMMARY

From a hemodynamic point of view, hypertension may be a manifestation of the operation of a defense mechanism of the peripheral circulation against a derangement of the governing mechanism of the heart tending toward increased cardiac output; or as a defense mechanism of the governing system of the heart against increased peripheral resistance in the peripheral circulation. In view of present knowledge concerning the governing system of the heart with respect to cardiac output, the latter possibility is most likely.

Flow of blood in arterioles and capillaries is laminar in character and conforms to Poiseuille's law. Factors controlling resistance to flow are enumerated and examined. Factors most likely to provide increased resistance to flow present in hypertension are increased viscosity of the blood or reduction in diameter of arterioles.

Determination of viscosity of blood is discussed. No reliable information concerning viscosity of blood in hypertension is at hand. Most investigators assume increased resistance to flow in hypertension to be a result of decreased arteriolar diameter. No direct experimental evidence has yet been obtained to sup-

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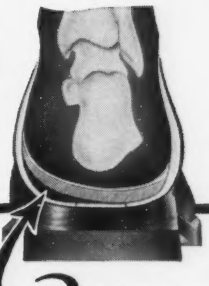

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port this assumption. If reduction in arteriolar diameter does obtain, it is not the result of an increase in neurogenic vasomotor tone.

The increased pulse pressure of hypertension is largely determined by decreasing distensibility of the arterial system with increasing pressure.

Trauma to the peripheral circulation in hypertension should correspond with the levels of diastolic blood pressure. Trauma to the heart in hypertension should correspond with levels of systolic blood pressure.

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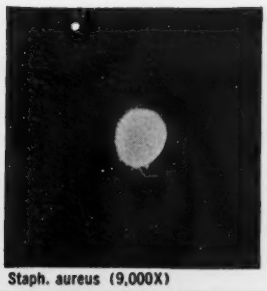
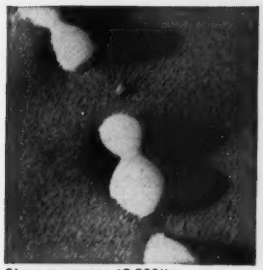
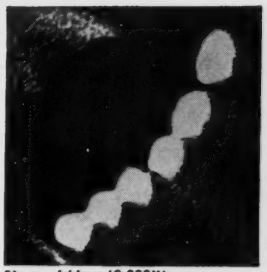


Staph. aureus (9,000X)



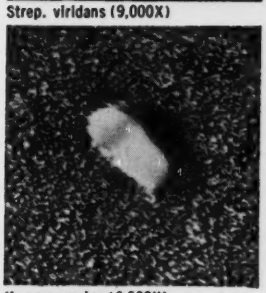
Strep. pyogenes (8,500X)



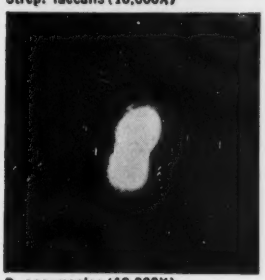
Strep. viridans (9,000X)

Strep. faecalis (10,000X)

E. coli (8,000X)

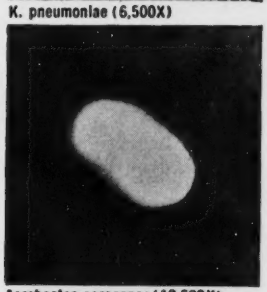


K. pneumoniae (6,500X)



D. pneumoniae (10,000X)

H. influenzae (16,000X)



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A request to Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York, will provide information on three courses to be offered there next month. The diagnosis and treatment of poisonings will be the subject of a course from December 5 through 7. A course on infertility will be offered on the same dates. Five days, beginning December 5, will be devoted to a study of pediatric cardiology.

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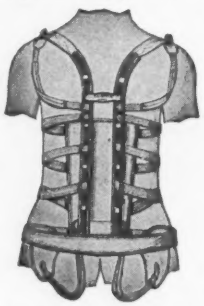

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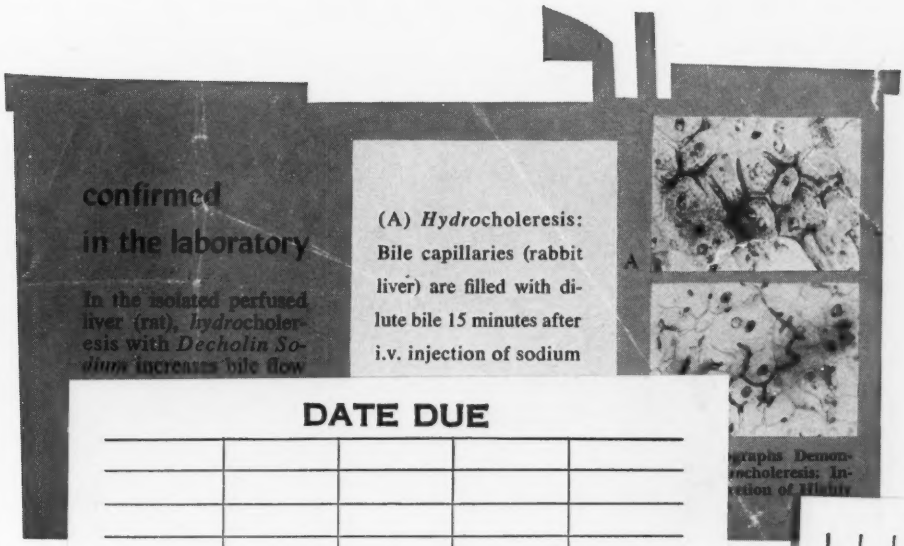

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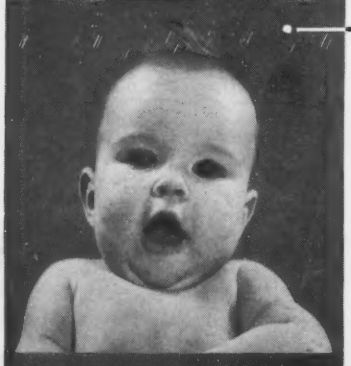

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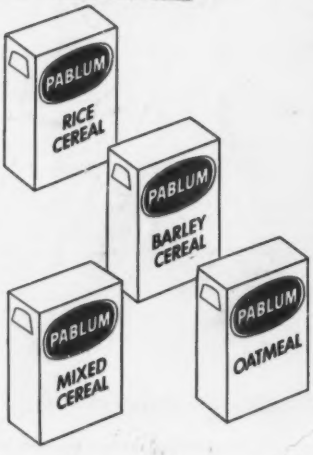

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